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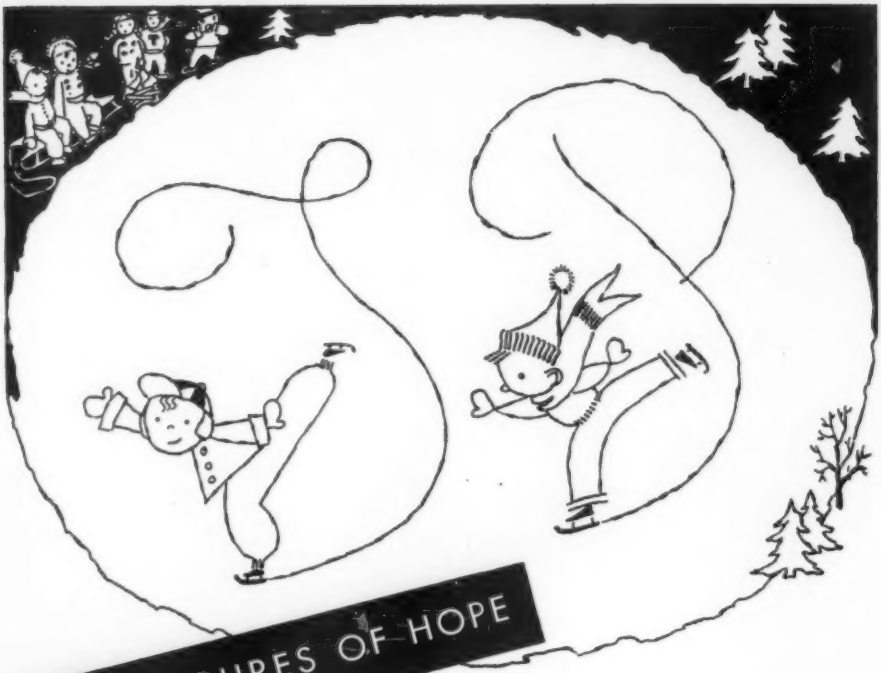

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(1) Organe, G.: Lancet, 1:773, 1949.
(2) Grob, D., Holaday, D. A. and Harvey, A. McG.: New Eng. J. Med. 241:812 and 816, 1949.
(3) Castillo, J. C., and de Beer, E. J.: Fed. Proc. Part 1 8:279, 1949.
(4) Castillo, J. C., Phillips, A. P. and de Beer, E. J.: J. Pharm. and Exp. Ther. 97:150, 1949.
(5) Spencer, C. H. and Cookley, C. S.: Med. Ann. Dist. Col. 19:132, 1950.
(6) Harris, L. C. and Dripps, R. D.: J. Anesthesiology 11:214, 1950.

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Dear Reader:

As PRESIDENT of the American Academy of Neurology, it is my privilege and pleasure to be the first to extend a welcome to all readers of this new journal, the first in the United States devoted exclusively to the most important subject of neurology.

Properly defined, neurology refers to that portion of medicine which deals with the diagnosis and treatment of symptoms and diseases related to or involving the nervous system. When one considers the many components of the nervous system, its importance to the adequate functioning of the individual as a whole as well as the separate organ systems, and the numerous common illnesses that are due to disturbed nervous system function, it soon becomes apparent that an adequate knowledge of neurology is urgent if one is to practice good medicine. Many illnesses seen daily by the physician implicate the nervous system either primarily or as an associated involvement and must be considered in the evaluation of patients, not only for diagnosis but also for prognosis and therapy. Thus, neurology must not be considered an unusually complicated, highly developed diagnostic specialty which is beyond the scope of the average general practitioner. It must be accepted as an integral part of the therapeutic program of the general field of medicine.

The American Academy of Neurology has felt for some time a need to stimulate more interest on the part of the medical profession in the field of nervous system disorders and to emphasize to them its importance. The treatment program for diseases of the nervous system has been expanding very rapidly, and it is imperative to have a means of communicating new therapeutic procedures to the entire medical profession. It was felt that such information could be conveyed best through a journal dedicated to the dynamic aspects of neurology. This journal, directed toward emphasizing the clinical aspects of this field in all its phases, would bring to the profession practical articles on diagnosis and reviews on all phases of current therapy.

With this in mind, the American Academy of Neurology presents its new journal, NEUROLOGY, with the hope that it will help American neurology take its proper place among the medical specialties, and stimulate better training, teaching, diagnosis and treatment in this field in the interest of better medicine and with greater benefit to the American public.

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CONTENTS — JANUARY-FEBRUARY — 1951

President's Message
A. B. BAKER, M.D. ..... *v*

The Past, Present and Future of Neurology in the United States
PEARCE BAILEY, M.D. 1

Cerebellopallidal Anisosthenia
ROBERT BING, M.D. 10

Pendulousness of the Legs as a Diagnostic Test
ROBERT WARTENBERG, M.D. 18

The Electroencephalogram in Intracranial Aneurysms
E. ROSEMAN, M.D., B. M. BLOOR, M.D., AND RICHARD P. SCHMIDT, M.D. 25

Spinal Cord Tumors with Minimal Neurologic Findings
FREDERICK P. MOERSCH, M.D., WINCHELL MC.K. CRAIG, M.D., AND LEE A. CHRISTOFERSON, M.D. 39

Role of Birth Injury and Asphyxia in Idiopathic Epilepsy
J. M. NIELSEN, M.D., AND CYRIL B. COURVILLE, M.D. 48

Polycythemia Vera and the Nervous System
DAVID R. JOHNSON, M.D., AND WILLIAM S. CHALGREN, M.D. 53

Newer Drugs in the Treatment of Parkinsonism
LEWIS J. DOSHAY, M.D., AND KATE CONSTABLE, M.D. 68

Treatment Review
Practical Considerations in the Treatment of Head Injuries
A. EARL WALKER, M.D. 75

Clinical Pathologic Conference
DISCUSSION BY D. E. DENNY-BROWN, M.D. 85

Editorial
RUSSELL N. DE JONG, M.D. 94

Book Reviews 95

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The Past, Present and Future of Neurology in the United States

Pearce Bailey, M.D.
Washington, D. C.

AN INTERPRETATION of important trends in the checkered past of American neurology is not a simple task. The problem springs from the fact that a good history of neurology never has been written. We have biographies of eminent neurologists which do not give the story of their times; we have accounts of important neurological discoveries which do not reflect the philosophic trends leading to their creation; and we have jumbled histories of neurology so confused with the history of psychiatry that it is difficult to identify one from the other. American neurology needs a Voltaire to interpret the meaning of its saga.

It seems surprising that no comprehensive longitudinal account has been given of the specialty devoted to study of the most central and perhaps the master tissue of the body and personality. This is less surprising, however, when one realizes that American neurology never has attained an unchallenged professional autonomy as a medical specialty. Continually vacillating as a satellite between internal medicine and psychiatry, neurology has had only partial glimpses of true autonomy. In fact, a struggle for a position of independence in the medical hierarchy appears to be the dynamic theme underlying the real story of American neurology. Let us briefly trace this principle during the various historical periods of neurology in order to evaluate it in terms of the present status and the future of neurology.

THE EARLY PERIOD (1862-1880)

The years from 1862 to 1880 may be regarded as the cradling period of American neurology, which was born during the Civil War. Many general practitioners who served in the army medical departments emerged as practicing neurologists. Conspicuous among them was William A. Hammond (1828-1900), who was appointed Surgeon-General of the United

From the department of neurology, Georgetown University.

Read at the first interim meeting of the American Academy of Neurology, Cincinnati, Ohio, April 14, 1950.

States Army, and S. Weir Mitchell (1829-1914), who operated a hospital for nervous diseases in Philadelphia (1862). The team of Hammond and Mitchell virtually placed neurology on the medical map of the United States, and they were towers of strength in its early growth.

The then new and rigorous neurologic enterprise began to sparkle in its activity, and superior medical minds were attracted to its ranks. The New York Neurological Society was founded in 1872 by a distinguished group, and three years later the American Neurological Association held its first meeting. The Journal of Nervous and Mental Disease, founded in 1874, provided an official organ of expression. During this period American neurologists had formed a solid nucleus for the expansion of their discipline within the framework of internal medicine, and they occupied a position of high prestige and influence among the medical intelligentsia.

At this time also the neurologists dabbled somewhat in psychiatry, but they remained aloof and independent of the institutional psychiatrists, or alienists as they were then called. Few of these neurologists were inclined to formulate a psychopathology. The early efforts of George M. Beard, who coined the term "neurasthenia", to establish a medical psychology were resisted—often with sarcasm.[1] After Beard presented his first paper at the second meeting of the American Neurological Association, W. A. Hammond remarked: "If the doctrine advanced by Dr. Beard was to be accepted, he (Beard) should feel like throwing his diploma away and following the theologians." Even J. J. Putnam, who later accepted most of the tenets of psychoanalysis, stated that he regarded "Beard's experiments as unscientific, because the emotions could not be isolated."

Briefly stated, the neurologists of this nascent period remained more or less anchored to internal medicine, for they were all products of medical wards. However, they functioned independently of psychiatry and had sown potent seeds for the development of neurology as a distinct medical specialty at the time when medical specialties were to be formed—at the beginning of the twentieth century.

THE SECOND PERIOD (1880-1900)

This period in the history of neurology is noted for: 1) addition of new members and fresh talent to the neurologic fold; 2) precision of a definite methodology in American neurology; and 3) gravitation of neurology from its original attachment to internal medicine more in the direction of psychiatry.

Many physicians of high intellectual calibre became neurologists during this era, as reflected by the fact that the possible membership of the

American Neurological Association doubled in 1887.[1] During this expansion, American neurology also had more precisely defined its methodology. Though modern neurology began with the work of Romberg (1840) and his followers, the early American school showed more clearly the influence of the neurologists of France, Cruveilhier, Vulpian, Duchenne of Boulogne, and Charcot and his pupils, whose methods were essentially morphologic being deeply rooted in structure. Following the lead of the French, American neurologists formulated a structural approach, emphasizing the description of distinct clinico-anatomical syndromes and giving less consideration to the problem of a disturbed physiology of the organism as a whole. They were becoming erudite diagnosticians of specific syndromes, but were paying little heed to the promulgation of a therapeutic program for their patients.

Another feature of the second period was the closer identification of neurologists with the study and practice of psychiatry. In 1883 two systematic treatises on mental disorders, the first to appear in the United States since Benjamin Rush's "Medical Inquiries and Observations upon the Diseases of the Mind," were written by neurologists—William A. Hammond and E. C. Spitka. This march into psychiatry was by the strictly organic route of neuroanatomy and neuropathology, originally sponsored by Griesinger and Meynert in Europe and championed in this country first by Spitka and later by Jacoby.[2]

The advance of neurologists into psychiatric practice largely took the form of a critical attack on the institutional psychiatrists for the latter's alleged isolationism, lack of research and hospital abuses. The most scathing indictment came from S. Weir Mitchell in 1894 in an address delivered at the fiftieth annual meeting of the American Medico-Psychological Association, later to become the American Psychiatric Association in 1921. The predominant position of neurologists in the practice of psychiatry at that time was accepted both by organized medicine and the lay public. At the end of the nineteenth century a psychiatrist almost had to be a neurologist to be respectable.

Thus, at the end of its second period of development, American neurology was approaching closely the highest peak of autonomy it was ever to attain. On the one hand it had formed a small but powerful group functioning independently within the framework of internal medicine, and on the other it had assumed a function of leadership and prestige in the teaching and practice of psychiatry. But, as we shall see later, it lacked essential prerequisites for true professional autonomy as a medical specialty.

THE THIRD PERIOD (1900-1917)

Neurology during the third period of its history in the United States was stimulated by new methodologies in its own field and by further expansion into the domain of psychiatry, but this time by a psychological rather than an organic approach. A fresh impetus was given in a new methodologic direction by the imprint left by Hughlings Jackson's concept of levels (1898) and by the work of Sherrington (1906), which revealed an immense potential for the investigation of the physiologic and dynamic functions of the nervous system.

Notable contributions were made to the neuron theory; to cortical localization in general and aphasia in particular; to vascular syndromes, especially the syndrome associated with occlusion of the posterior inferior cerebellar artery; to focal epilepsy; and to the structure and function of the endocrine glands. Significant during this period was an elucidation of the problem of neurosyphilis. The discovery of a specific test by Wassermann (1906), the introduction of arsphenamine by Ehrlich (1910), and most of all the discovery by Moore and Noguchi (1911) of the presence of spirochetes in the brains of paretics enabled neurologists, through their clinicopathological studies, to identify tabes dorsalis and general paresis as syphilitic diseases. Furthermore, it presented them with a large group of patients to treat therapeutically if they cared to do so. The work of von Economo (1917) and the epidemic of encephalitis lethargica opened still another field for investigation.

During this period, also, neurologists again approached psychiatry, not by the organic route as previously, but by way of psychopathology influenced by the adept presentations of J. J. Putnam, Dana, Morton Prince, and Jelliffe. Putnam[3] was the neurologic spokesman for psychoanalysis; Dana[4] advocated that neurology expand in the direction of psychology and sociology; Morton Prince[5] conceived the future of neurology as an investigation of the subconscious; and Jelliffe, the principal neurological commentator of his day, spoke of symbolic neurology.

During this period neurology probably reached the zenith of its autonomy as a medical specialty. Its scope had been enlarged by discoveries and new avenues of investigation had been opened. It had penetrated deeply into the practice of psychiatry from a psychological approach and had not been absorbed by psychiatry. Nevertheless, as a specialty it was vulnerable. Neurology still lacked an over-all leadership and its organization had no central theme. Neurology was still isolated sectionally in the face of a rapidly expanding geographic distribution of population. Neurologists still remained primarily diagnosticians and showed little interest in the total care of their patients, which was left

to others. Neurology was vulnerable therefore—vulnerable to an attack which came from several directions in the next period of its history.

THE FOURTH PERIOD (1917-1945)

The fourth period should be called the period of neuropsychiatry. As a practical military expedient during World War I, neurology and psychiatry, neurologist and psychiatrist, were united under the compound terms of "neuropsychiatry" and "neuropsychiatrist," respectively. In 1917 at the time of the establishment of the Division of Neurology and Psychiatry in the Surgeon-General's office under a neurologist, army neurologists were mobilized who had office practice experience in the treatment of the psychoneuroses, but little knowledge of the psychoses. Psychiatrists, who were for the most part institutional administrators oriented in the psychoses, lacked experience in neurology and in the management of the psychoneuroses. Since functional nervous disorders were the number one medical problem of the war, it became essential to pool these divergent backgrounds of experience into a single operating unit. This was accomplished by giving supplementary training to both neurologists and psychiatrists in areas where they were defective and uniting them under the hybrid heading of "neuropsychiatry."[6] In the military setting this unification plan worked well.

The newly created military neuropsychiatry soon ramified into civilian teaching and practice. In spite of sporadic resistance, chiefly from psychiatry,[7] it had the strong backing of J. Ramsey Hunt[8] for neurology and Adolph Meyer[9] for psychiatry. Its acceptance became widespread, reaching a peak in the nineteen thirties, after which it began to decline, only to be reactivated by the mobilization of World War II.

It appears likely that the neuropsychiatric movement in the United States did more to set neurology back in its bid for professional autonomy than any other single development in its history. This movement split neurologically trained psysicians into two camps, neurologists and neuropsychiatrists, which tended to deplete them as a group. Moreover, they lost further professional identity by being eclipsed by a rising multitude of psychologically minded psychiatrists who also were called neuropsychiatrists and who eventually assumed command of the domain of neuropsychiatry.

While being disjointed under the shroud of neuropsychiatry, neurology experienced reverses from other quarters. Following the discovery of pneumoencephalography and ventriculography by Dandy (1919), the already budding specialty of neurologic surgery burst into full bloom under the astute and progressive leadership of Harvey Cushing. The

new, young, spirited and closely knit group of neurosurgeons graduated way above the level of surgical technicians. They entered aggressively the field of neurologic research, especially along neurophysiologic lines, which had been neglected by the clinical neurologists; they were therapeutically minded in contrast to the traditional neurologist who began to assume a reactionary tinge; and in some instances, the neurosurgeons challenged the neurologist's specialized talent in neurologic diagnosis.[10]

Consequently, at the end of World War II, the clinical neurologist found himself out of harmony with the trend of the times, and was confused by the glare of a scintillating psychologic age. In practice, he was crowded by the psychiatrist on the one hand and by the neurosurgeon on the other. Divided and weakened by the neuropsychiatric movement, and always having lacked organization under a unified leadership with a constructive program of public relations, the clinical neurologists found it difficult to fall back on the treatment of neurologic diseases which, in the scramble for psychiatric practice, they had turned over to the pediatrician, orthopedist, dermatologist and internist. Moreover, the neurologist had never taken initiative in devising any projects for the rehabilitation of chronically disabled neurologic patients. The specialty continued to suffer from geographic isolationism. Even as late as 1948 there was only one diplomate in neurology per 1,488 physicians in the southeastern states and one per 1,949 in the southwestern states, as compared to one diplomate per 312 physicians in the northeastern states.[11]

Paralleling these reverses in the practice of neurology, there had been a corresponding diminution of prestige. During World War II, unlike World War I, no neurologist occupied any top position in the departments of neuropsychiatry of the Army, Navy or Public Health Service. Immediately following the war no neurologist held any post on any policy-making board of the Armed Forces, the Public Health Service, the Veterans Administration or National Research Council, though psychiatrists and neurosurgeons were in such positions. As of 1949, not a single grant-in-aid or training stipend under the authority of the National Mental Health Act had been given for training neurologists, though many had been given for training psychiatrists. From available data it is evident that medical schools as a whole have made little progress in the teaching of neurology during the past twelve years.[11, 12] Recently, most of the surplus of medical school budgets has been absorbed by neurologic surgery with its therapeutic approach and by psychiatry with its huge social welfare program which has received strong public support.

At the close of World War II, therefore, it appeared that neurology, particularly clinical neurology, had reached its lowest ebb.

THE PRESENT STATUS

In spite of an apparent decline of neurology as a medical specialty as outlined above, there are other factors to be considered in its recent history and present setting which indicate that neurology has not been reduced to extinction.

To begin with, there is still a basic interest in the study and practice of neurology as evidenced by replies to specially devised questionnaires for testing interest in neurology, sent out to 900 diplomates certified either in neurology alone or in both psychiatry and neurology prior to July 1947. Seventy-three per cent of the 521 replies received indicated an interest in neurology not subordinate to any interest in psychiatry.[13]

Secondly, even with the numerous reverses in neurology encountered during the fourth period of its history (1917-1945), there has been a steady growth in the number of hospitals approved for training in neurology by the Council on Education of the American Medical Asscciation. The number of these approved hospitals rose from 14 in 1935 to 68 in 1949, almost a fivefold increase. The increase in number of hospitals approved for training in neurology approximates proportionately the number of hospitals approved for training in psychiatry and internal medicine during the same period. Along with this rise in the number of approved hospitals, there has been an unprecedented growth of activity in the basic sciences of neurology, particularly along neurophysiologic lines. Opportunities provided by this expansion of neurophysiology have been exploited far more by neurosurgeons than by neurologists. However, propitious opportunity is at hand for neurologists to close the gap that now exists between the neurologic laboratory and the neurologic clinic.

Thirdly, World War II brought forth a large number of neurologically disabled veterans who have been promised by law first-class medical care. As a result, the Veterans Administration has developed the largest single neurological service ever known.[14] The number of neurologically disabled veterans from World War II exceeds proportionately the number from World War I, since new drugs and modern surgical techniques saved the lives of many men with similar neurologic disorders who died in World War I. Indeed, over one-third of the neuropsychiatric patient census in general hospitals of the Veterans Administration is comprised of neurologic cases. In special categories of the casualties of World War II there are about 20,000 craniocerebral injuries, almost 3,000 paraplegics and 1,000 post-traumatic aphasic patients. Approximately 50,000 epileptics come under the auspices of the Veterans Administration.

To meet this large demand, the Veterans Administration has employed over 200 neurologists, has established fourteen approved neurologic centers affiliated with medical schools, and has set up specialized programs in epilepsy, aphasia, spinal cord injuries, neurologic rehabilitation and electroencephalography.

There are now about 50 Veterans Administration residents in neurology, who are being trained not only in diagnostic aspects of neurology, but in neurologic therapeutics as well. It is hoped that a new generation of therapeutically-minded neurologists capable of taking over the complete management of neurologic disorders will be developed in this way. The program of the Veterans Administration has provided a new stimulus for the growth of neurology and a new demand for qualified neurologists.

THE FUTURE

These positive trends in the present status of neurology might well be coordinated to provide the impetus for a renaissance of neurology in the near future. However, in order that such a renaissance reach maturity, it is essential to correct the many weaknesses which have pervaded the entire history of neurology and blocked its destiny toward professional autonomy. The principal weaknesses may be summarized as: 1) Lack of organization of the specialty along strategic lines; 2) Geographic sectionalism; and 3) Absence of a constructive program for neurologic therapeutics. Steps are being taken to overcome these deficiencies, however.

The American Academy of Neurology, founded in 1948, has already gone far in a program for the dynamic reorganization of neurology. Its special committees have stressed the importance and needs of neurology as a specialty in medical education and government agencies, and are formulating a sound policy of public relations. In this effort the Academy is being aided by a new lay society, The National Society of the Study and Treatment of Diseases of the Nervous System, incorporated at St. Paul, Minnesota, which will subsidize worthy projects for neurologic research and the training of neurologists.

The scope of the Academy is nationwide and hence antagonistic to the geographic sectionalism which always has hemmed in the neurology of the past. It should be recalled that the early American neurologists were all aristocrats, originating for the most part from the northeastern section of the United States and guided by the principles of rugged individualism. There were no middle or lower classes in the neurology of the early days. This system may have been ideal for the founding of neurology in the last quarter of the nineteenth century, but it cannot be applied effectively to our present widely diffuse population and social

ideology where disciplines are dependent on a united front and mass movements in order to survive. Neurology needs a progressive middle class and the Academy, by virtue of its organizational plan, is equipped to help develop such a group.

The time has come for neurology as a specialty to assume responsibility for the total medical treatment of neurologic patients, both for the sake of the patients and in the interest of public welfare. The pilot program in neurologic rehabilitation activated by Doctors A. B. Baker and J. R. Brown[15] has opened an immense new vista of therapeutics for neurologic patients. Similar programs are now beginning to shape in civilian medicine.

In September 1949, at the Fourth International Neurological Congress, one half day of the sessions was devoted to a discussion of the present status of neurology in all countries. A resolution was passed by acclamation calling for a recognition of neurology as an independent dynamic specialty, and further resolving that all medical therapies dealing with the nervous system be considered and maintained as the primary responsibility of neurologists. An international committee was then appointed to implement this resolution throughout the world.

These various lines of positive development appear to be converging to a point of departure for a true renaissance of neurology. We have the raw material, we have the tools, and finally we have the beginnings of a sound organization of the specialty.

REFERENCES

1. Jelliffe, S. E.: Fifty years of American neurology, in Semi-centennial Anniversary Volume of the American Neurological Association (1875-1924), Albany, New York, Boyd Printing Company, 1924, pp. 386-438.
2. Jacoby, G. W.: Exact and inexact methods in neurology and psychiatry, J. Nerv. & Ment. Dis. 42:660, 1915.
3. Putnam, J. J.: Addresses on Psycho-Analysis, London, International Psycho-analytical Press, 1921.
4. Dana, C. L.: The future of neurology, J. Nerv. & Ment. Dis. 40:753, 1913.
5. Prince, Morton: American neurology of the past—Neurology of the future, J. Nerv. & Ment. Dis. 42:445, 1915.
6. Medical Department of the United States Army in the World War: X: Neuropsychiatry, Washington, D. C., War Department, 1929.
7. May, J. V.: The establishment of standards by the association, Am. J. Psychiat. 90:1, 1933.
8. Hunt, J. R.: The domain of neuropsychiatry and the training of the neuropsychiatrist, Arch. Neurol. & Psychiat. 31:1078, 1934.
9. Meyer, Adolph: Inter-relations of the domain of neuropsychiatry, Arch. Neurol. & Psychiat. 8:111, 1922.
10. Bailey, Percival: The practice of neurology in the United States of America, J. A. Am. M. Coll. 21:281, 1946.
11. Pollock, L. J.: Report of the committee on public relations, Tr. Am. Neurol. A. 74:16, 1949.
12. Viets, H. R.: Neurology—Past and present, J. A. M. A. 109:399, 1937.
13. Bailey, Pearce: The present outlook for neurology in the United States, J. A. Am. M. Coll. 24:214, 1949.
14. Bailey, Pearce: Program for the activation of neurology under the Veterans Administration, J. A. M. A. 134:1283, 1947.
15. Baker, A. B., and Brown, J. R.: Rehabilitation of Chronic Neurologic Patients, Veterans Administration Pamphlet 10-29, Washington, D. C., U. S. Government Printing Office, 1949.

Cerebellopallidal Anisosthenia

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In 1886 the British physiologist Gaskell[1] made a distinction between two antagonistic groups of nerves, the visceral and the vascular. To be sure, it was Claude Bernard who made the first sharp distinction between the visceral and the vascular nerves, but we are indebted to Gaskell for discrimination between the vegetative, both visceral and vascular, nerves of "lateral" and "collateral" origin and for the stress laid upon their functional antagonism.

Gaskell found that neurons coming from cells of the "lateral" ganglionic system subserve vasoconstriction, acceleration of the heart, and contraction of ring muscles in the cavities; whereas neurons coming from the "collateral" accumulations of cells subserve vasodilation, deceleration of the heart, and contraction of longitudinal muscles.

Further consideration of the antagonism in regulation of gland function, blood pressure and movements of the pupil has enriched the thesis of Gaskell. On it is based the Eppinger and Hess[2] theory of sympathicotonia and vagotonia. Of course, pure cases of the Eppinger and Hess syndrome do not exist. However, there is certainly an amphotonia in which the whole vegetative nervous system is hyperirritable, and there is also a neurotonia with predominant sympathicotonic or vagotonic features. The distinction made by Dale[3] between cholinergic and adrenergic persons corresponds essentially to these last two groups. Kroetz[4] and von Beznák,[5] in continuation of the work of Loewi,[6] assumed the existence of an autacoid regulation. Here the function of an organ or of cells is governed by two mechanisms, one promoting, and the other retarding.

In the vegetative nervous system there exists a marked antagonism. This has been unmistakably established. It is antagonism between the action of sympathin (Cannon[7]) and of acetylcholin. Sympathin is most probably identical with adrenalin and is released at the end organs of the sympathetic nerves. Acetylcholin is released from the parasympathetic

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nervous system. The two variants of "vegetative dystonia" are the real prototypes of nervous disturbances which stem from changes in the normal state of equilibrium. This normal state is called "isosthenia." When this balance is disturbed, an "anisosthenia" results.

In the regulation of internal secretion, too, antagonistic hormones are mutually attuned in a most delicate manner. It is all important that their balance be maintained. Only by maintenance of this balance can a normal state be achieved and sustained. Furthermore, the close relationship between the whole vegetative nervous system and the endocrine system must always be kept in mind.

From this it may be assumed that regulation of the motor nervous system also may be disturbed in a similar way and anisosthenia result clinically.

It has been found that in the cerebellum disturbance of balance of innervation between its different parts plays a decisive role. The experimental work of Bolk,[8] van Rynberk,[9] Rothmann[10] on animals has led us to assume that in the cerebellum different parts of the body are represented in a way similar to the motor cortex of the brain. The clinical investigations of Bárány,[11] Thomas,[12] Thomas and Durupt[13] warrant the following conclusions: There are definite and circumscribed direction centers for outward tonus and for inward tonus; for downward tonus and for upward tonus. This arrangement influences the Bárány test for each individual limb. If such a direction center is destroyed or considerably damaged, antagonistic mechanisms come into action and past-pointing to the opposite direction results. It is true that the existence of the direction centers for inward and upward tonus seems to be less well established, and their site not so well localized as that of the centers for outward and downward tonus.[14] It is true, as Goldstein[15] has shown, that the same past-pointing, predominantly abduction and extension, results from cerebellar lesions of different sites. Goldstein expressed doubt as to whether past-pointing is an appropriate test upon which to base the exact topical diagnosis of cerebellar lesions, but these objections concern detail. They do not question the necessity of cerebellar isosthenia for the harmonious distribution of muscular tonus over diverse regions of our motor system. Examination of cerebellar patients on a movable table reveals disturbances in static adaptation and demonstrates the importance of precise "contre-balancement" for the correct functioning of the "statotonus" (Edinger[16]).

While the concept of cerebellar anisosthenia has found widespread recognition with regard to similar pathophysiologic mechanisms in the

realm of the myostatic nervous system, we have not gone beyond the theoretical stage. Such a theory is very plausible, however. In 1926 attention was drawn[17] to some reversible forms of spasmodic torticollis, head nodding, blepharospasm, etc., which can be best interpreted as manifestations of a transient extrapyramidal anisosthenia. These morbid conditions may be attributed to passing disturbances in the reciprocal balance between various areas of the extrapyramidal nervous system.

Some postencephalitic syndromes demand similar interpretation. Their organic character, even in cases without postmortem verification, is beyond any doubt. Unlike the well known parkinson type of extrapyramidal rigidity, in these syndromes there must be alteration in the tonus balance of single muscles or of muscle groups. These circumscribed and selective alterations in the balance of muscle tonus lead to marked postural deformities. Sometimes these syndromes appear as outspoken torsion dystonias,[18] as torticollis-like syndromes, or as other localized spasms.[19, 20, 21] In dystonias due to such lesions, the outspoken element of rigidity accounts for the fact that they are more dynamic than their cerebellar analogues. On the other hand, attempts of Mingazzini,[22] Mills and Spiller,[23] C. and O. Vogt[24] to establish a functional localization within the striatum comparable to the cerebellar direction centers must be regarded as premature.

A quantitative balancing of antagonistic elements takes place not only inside the cerebellar and myostatic apparatus. The mutual physiologic coordination of the cerebellar system and the extrapyramidal system brings about signs and syndromes which document the breaking up of isosthenia between these two systems. In the following we will speak of such cerebellopallidal anisosthenias. They are not only of great theroretic interest, but give us practical and valuable diagnostic clues.

When we compare the overall picture of the syndrome produced by destructive lesions of the cerebellum with that produced by destructive lesions of the paleostriatum and when we consider the resulting changes in tonus, we are struck by the sharp antagonism between these two syndromes. In the light of present knowledge this is not difficult to understand (Bing).[25] We know that the cerebellar tonus is a reflex phenomenon. Its afferent path consists of elements of the posterior roots and the adjoining spinocerebellar fibers. The red nucleus lies in its efferent path. We know this nucleus to be the end station of the superior cerebellar peduncle, as well as the starting point of the rubrospinal tract which leads to the anterior horn cells of the spinal cord. Through the ansa lenticularis, the globus pallidus exerts a restraining influence on the red nucleus. A lesion of the globus pallidus, therefore, brings about an increase

in cerebellar tonus. In this way what is called extrapyramidal rigidity results. As seen particularly in the parkinson syndrome, this extrapyramidal rigidity is symptomatically different from pyramidal spasticity. This can easily be explained on the basis of the different anatomical sites of the lesions. However, extrapyramidal rigidity has many points in common with Sherrington's[26] decerebrate rigidity. The similarity between extrapyramidal and decerebrate rigidity is unmistakable and probable. Wilson[27] and Mourgue[28] even tried to consider these two conditions as identical. This view, however, must be rejected since, among other reasons, the pharmacologic response is different in each condition. Scopolamine, which reduces extrapyramidal rigidity very markedly, is without effect upon experimental decerebrate rigidity. It was Delmas-Marsalet[29] who first demonstrated this.

It is an incontestable fact that a general antagonism exists between lesions of the cerebellum which diminish muscle tonus, and lesions of the paleostriatum which increase this tonus. This antagonism manifests itself by clinical changes in tonus. Of these, three are most important:

(1) There is a striking contrast between induced tonus seen in cerebellar hypotonia and that seen in pallidal hypertonia. While the work of Magnus and de Kleijn[30] on reflexes was concerned essentially with function of the labyrinth and especially of the otoliths, studies of induced tonus by Delmas-Marsalet,[31] Goldstein,[32] Hoff and Schilder,[33] Zingerle[34] contributed much to our knowledge of pathophysiology of the cerebellum. The position test is of particular importance here. In this test, the examiner observes the involuntary changes of position which occur in the horizontally outstretched arms of the patient who closes his eyes. Usually there is no deviation in the arms in the normal. However, in 20 percent of normal persons a minimal upward and outward movement may occur. In unilateral affections of the cerebellum there is a marked and constant homolateral upward and outward movement. In contradistinction to this, in extrapyramidal affections there is an outspoken downward and inward movement. This has been observed in at least two-thirds of cases of post-encephalitic parkinsonism and paralysis agitans. The different results of the position test demonstrate the existing antagonism between the pallidal and cerebellar nervous systems.

(2) Lotmar[35] found that in unilateral lesions of the cerebellum the patient, judging with closed eyes equal weights put into his hands, always underestimates the weight on the affected side. The weight on that side seems lighter to him. The finding of Lotmar has been confirmed by Goldstein,[36] Maas,[37] and others. Some critique of Lotmar's view can be obviated. Bing[14] found that a homolateral impairment of this baryesthesia, or

sensibility for weight, documents itself more often as impairment of ability to distinguish weight differences put in either hand. While in Lotmar's test an equal weight is put into each hand and the patient is asked whether there is a difference in the two weights, Bing's test consists of putting different weights into each hand to determine the minimal difference in weight discernible by the patient. Patients with unilateral affections of the cerebellum showed on examination that the homolateral impairment of baryesthesia could be detected by the latter test much more easily and more frequently than by the test of Lotmar. These were all cases in which the cerebellar involvement was later proven at operation or autopsy. A normal patient could easily distinguish a weight difference of from 15 to 20 grams, whereas those with cerebellar affection could hardly notice weight differences of from 50 to 100 grams. In the evaluation of Lotmar's test it must be considered that a normal righthanded person has a tendency to underestimate weight in his right hand, and vice versa. It must also be taken into consideration that in the rare cases of irritative lesions (bleeding on the surface of the brain or serous meningitis of the posterior fossa), there may be an overestimation of weight on the affected side.[38] Despite all this, the high diagnostic value of Lotmar's test remains incontestable. Bearing in mind the results of Lotmar's test in which there is an underestimation of weight on the side of the cerebellar lesion, it is highly significant to find that in unilateral postencephalitic parkinsonism the patient overestimates weights placed in his affected hand.[39] This has been found in 75 to 80 per cent of cases. If a box containing 140 grams of shot is put into the affected hand of a patient with unilateral parkinsonism, he regularly finds this much heavier than a box of the same size filled with 180 grams of shot and placed in his normal hand.

(3) Luciani[40] has demonstrated that in the experimental animal deprived of the cerebellum motor incoordination makes itself evident by dysmetria. In 1907, Bing[41] proved that the same disturbance occurred when the spinocerebellar tracts had been severed. Thomas and Jumentié[42] demonstrated dysmetria in patients with cerebellar lesions. In impressive illustrations they showed that when such a patient grasps an object or lets it go, the hand is opened too wide and in quite an unnecessary and unsuitable manner. Excessive, hypermetric movements also occur in the heel-knee test, even if this is performed with the eyes open. Exactly the opposite, a hypometria is found in lesions of the paleostriatum, particularly in parkinsonism and most clearly in postencephalitic parkinsonism.

These quantitative disturbances of the coordination of movement reveal themselves very delicately in the size of the handwriting. When, after the great epidemics of encephalitis at the beginning of the twenties,

patients with parkinsonism appeared in large numbers and extrapyramidal micrographia was noticed.[43, 44, 45, 46] When such a patient starts to write, his first letters are of normal size, but this size constantly diminishes until the result is what the French call "écriture lilliputienne." To decipher such illegible scribbling a magnifying glass may be necessary. Quite the opposite of this extrapyramidal micrographia is cerebellar megalographia. In 1923 this was found in a case of gliosarcoma of the vermis confirmed at autopsy.[43] Zimmerli,[47] Petitpierre,[48] et al. discussed the subject later. In megalographia, the size of the letters increases rapidly as the patient continues to write and may reach excessive dimensions. This is seen less often, however.

In this connection the author would like to stress the fact that he has never observed a positive Schilder's[49] test for bradyteleokinesis in cerebellar affections. When this test is positive, the intended movement stops short of its goal. However, it has been found positive innumerable times in the parkinsonism syndrome.

In the cerebellar syndrome some signs may be encountered which are identical with those seen in the pallidal syndrome. This may be the result of disturbances in the mechanism of either apparatus. They are attuned to each other. The clinical manifestations depend on whether the deviation from the isosthenic balance takes place on the plus or on the minus side. Adiadochokinesis, catalepsy in which the patient keeps a limb in a position which has been brought on passively, and tremor may serve as examples of clinical manifestations common to both syndromes. However, here we must consider that concomitant mesencephalic lesions may exist.

Our knowledge of cerebellopallidal anisosthenias has a practical application. It is, of course, highly desirable to detect threatening parkinsonism in former encephalitis patients at the earliest possible moment. The prodromal stage in postencephalitic parkinsonism may extend over many years. It is usually recommended that one look for a slight reduction in the pendulousness of one arm in walking, for any slowing up of motility which is at first inconspicuous and easily overlooked, for reduction of facial expressiveness, for slight increase in the flow of saliva, etc. Based on our very extensive experience with epidemic encephalitis in Switzerland, we consider the signs of impaired equilibrium of the cerebellopallidal innervation as danger signals of postencephalitic parkinsonism. These signs are particularly reliable both diagnostically and prognostically. Periodic examinations of patients who have suffered an attack of encephalitis epidemica show this in a very impressive manner. It is particularly the slow transition of the position test from normal to that seen in extrapyramidal disease which constitutes a premonitory sign of oncoming

parkinsonism. In patients who have been followed for some time, a measurable tendency toward reduction in the size of handwriting is much less common. A tendency toward overestimation of weight is seen in such patients somewhat more often, especially when this tendency is unilateral. When there is a suspicion of an incipient Parkinson's disease, these tests for anisosthenia render valuable diagnostic help.

It is known that in tumors of the basal ganglia, localized striatal signs are often absent and clinical pictures of parkinsonism are rare. On examination for the arm deviation test in these cases, we most often find a tendency for the arms to deviate downward and inward.

It is true that we have no extrapyramidal type of multiple sclerosis which could serve as a diagnostic counterpart to the common cerebellar type. However, there are cases in which the tests for cerebellopallidal anisosthenia point to the involvement of the extrapyramidal nervous system in multiple sclerosis. This involvement has often been seen at autopsy. In any event, these tests are much more often positive than the so-called extrapyramidal reflexes.

REFERENCES

1. Gaskell, W. H.: On the structure, distribution and function of the nerves which innervate the visceral and vascular systems, J. Physiol. 7:1, 1886.
2. Eppinger, H., and Hess, L.: Zur Pathologie des vegetativen Nervensystems, Ztschr.f. klin.Med. 67:345, 1909.
3. Dale, H.: Transmission of nervous effects by acetylcholine, Bull. New York Acad. Med. 13:379, 1937.
4. Kroetz, C.: Allgemeine Physiologie der autonomen nervösen Correlationen, in Bethe, et al.: Handbuch der Normalen und Pathologischen Physiologie, Berlin, J. Springer, 1931, vol. 16, pt. 2, pp. 1729-1821.
5. von Beznák, A.: Die autacoide Aktivität des venösen Blutes von sezernierenden Submaxillardrüsen, Arch. f. d. ges. Physiol. 229:719, 1932.
6. Loewi, O.: Über humorale Übertragbarkeit der Herznervenwirkung, Arch.f.d.ges. Physiol. 189:239, 1921, and 193:201, 1922.
7. Cannon, W. B.: The story of the development of our ideas of chemical mediation of nerve impulses, Am. J. M. Sc. 188:145, 1934.
8. Bolk, L.: Das Cerebellum der Säugetiere, Jena, G. Fischer, 1906.
9. van Rynberk, G.: Die neueren Beiträge zur Anatomie und Physiologie der Kleinhirns des Säuger, Folia neuro-biol. 1:535, 1908.
10. Rothmann, D.: The symptoms of cerebellar disease and their significance, Internat. Cong. Med. London, 17:23, 1931.
11. Bárány, R.: Localisations dans l'écorce de l'hémisphère du cervelet humain, Rev. d'oto-neuro-opht. 2:23, 1924.
12. André-Thomas: Pathologie du cervelet, in: Roger-Widal-Teissier: Nouveau Traité de Médecine, Paris, Masson et Cie, 1925, vol. 19, pp. 755-980.
13. Thomas, A., and Durupt, P.: Localisations cérébelleuses, Paris, Vigot Frères, 1914.
14. Bing, R.: Kleinhirn, in: Mohr and Staehelin: Handbuch der Inneren Medizin, ed. 3, Berlin, J. Springer, 1939, vol. 5, pt. 1, pp. 74-92.
15. Goldstein, K.: Erkrankungen des Kleinhirns, in: Mohr and Staehelin: Handbuch der Inneren Medizin, ed. 2, Berlin, J. Springer, 1925, vol. 5, pt. 2, p. 335.
16. Edinger, L.: Anatomisch-physiologische Einleitung der Nervenkrankheiten, in Kraus and Brugsch: Spezielle Pathologie und Therapie Innerer Krankheiten, Berlin, Urban and Schwarzenberg, 1924, vol. 10, pt. 1, pp. 1-98.
17. Bing, R.: Hypercinésies organiques et psychogènes, Schweiz. Arch.f.Neurol.u. Psychiat. 18:163, 1926.
18. Bing, R., and Schwartz, L.: Über Torsiondystonien und verwandte Symptomen-

komplexe im Gefolge von Encephalitis epidemica, Schweiz. Arch.f.Neurol.u.Psychiat. 14:80, 1924.

19. Cassirer, R.: Halsmuskelkrampf und Torsionsspasmus, Klin. Wchnschr. 1:53, 1922.
20. Paulian, E. D., and Grigoresco, D.: Sur un état de Parkinsonisme rappelant un syndrome analogue du spasme de torsion, Rev. neurol. 38:1403, 1922.
21. Marie, P., and Lévy, G.: Plicature du cou et du tronc par encéphalite épidémique se rapprochant du "spasme de torsion," Rev. neurol. 38:570, 1922.
22. Mingazzini, G.: Das Linsenkernsyndrom, Ztschr. f. d. ges. Neurol. u. Psychiat. 8:85, 1912.
23. Mills, C. K., and Spiller, W. G.: The symptomatology of lesions of the lenticular zone with some discussion of the pathology of aphasia, J. Nerv. & Ment. Dis. 34:558, 1907.
24. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. f. Psychol.u.Neurol. 25:627, 1920. Ergänzungsheft, 3.
25. Bing, R.: Kompendium der topischen Gehirn- und Rückenmarksdiagnostik, ed. 13, Basel, B. Schwabe, 1948. p. 247 and p. 249.
26. Sherrington, C. S.: Decerebrate rigidity, and reflex coordination of movements, J. Physiol. 22:319, 1897-1898.
27. Wilson, S. A. K.: On decerebrate rigidity in man and the occurrence of tonic fits, Brain 48:220, 1920.
28. Mourgue, R.: Le syndrôme clinique de la rigidité décérébrée de S. A. K. Wilson étudié dans un cas de spasme de torsion consécutif à l'éncephalite épidémique, Schweiz. Arch. f. Neurol. u. Psychiat. 11:163, 1922.
29. Delmas-Marsalet, P.: Les réflexes de posture élémentaires, Paris, Masson & Cie., 1927.
30. Magnus, R., and de Kleijn, A.: Die Abhängigkeet des Tonus der Extremitätenmuskeln von der Kopfstellung, Arch. f.d. ges.Physiol. 145:455, 1912.
31. Delmas-Marsalet, P.: Contribution expérimentale à l'étude des fonctions de noyau caudé, Bordeaux, Gounouilhou, 1925.
32. Goldstein, K.: Das Kleinhirn, in: Bethe, et al.: Handbuch der Normalen und Pathologischen Physiologie, Berlin, J. Springer, 1927, vol. 10, pp. 222-317.
33. Hoff and Schilder: Die Lagereflexe des Menschen, Vienna, J. Springer, 1927.
34. Zingerle, H.: Automatosesyndrom bei linksseitger Stirnhirnerkrankung, Ztschr. f.d.ges.Neurol.u.Psychiat. 145:249, 1933.
35. Lotmar, F.: Bemerkungen zur Adiadochokinese und zu den Funktionen des Kleinhirns, Cor. Bl.f.schweiz.Aerzte 43:1455, 1913, and 43:1457, 1913.
36. Goldstein, K.: Über Störungen der Schwereempfindung bei gleichseitiger Kleinhirnaffektion, Neurol. Centralbl. 32: 1082, 1913.
37. Maas, O.: Störung der Schwereempfindung bei Kleinhirnerkrankung, Neurol. Centralbl. 32:405, 1913.
38. Goldstein, K., and Reichmann, F.: Beiträge zur Kasuistik und Symptomatologie der Kleinhirnerkrankungen, Arch.f. Psychiat. 56:466, 1916.
39. Bing, R.: Sémiologie des affections cérébelleuses, Schweiz.Arch.f.Neurol.u.Psychiat. 16:3, 1925.
40. Luciani, L.: Das Kleinhirn, in: Asher, L., and Spiro, K.: Ergebnisse der Physiologie, vol. 3, pt. 2, pp. 259-388, 1904.
41. Bing, R.: Die Bedeutung der spino-cerebellaren Systeme, Wiesbaden, J. Bergmann, 1907.
42. André-Thomas, and Jumentié: Sur la nature des troubles de la motilité dans les affections du cervelet, Rev. neurol. 17: 1309, 1909.
43. Rossi, O.: Note cliniche sull'encefalite epidemica etc., Riv.di.pat.nerv. 27:135, 1922.
44. Schnyder, L.: A propos de la micrographie postencéphalitique, Rev. méd. de la Suisse Rom. 63:705, 1923.
45. Bing, R.: Ueber einige bemerkenswerte Begleiterscheinungen der "extrapyramidalen Rigidität" (Akathisie-Mikrographie-Kinesia paradoxa), Schweiz.med.Wchnschr. 4:167, 1923.
46. Froment, F.: De la micrographie dans les états Parkinsoniens postencéphalitiques et des conditions qui sont susceptibles de la modifier, Rev. neurol. 37:637, 1921.
47. Zimmerli, E.: Beiträge zur Symptomatologie der Kleinhirnerkrankungen, Deutsche Ztschr.f.Nervenh. 76:251, 1923.
49. Schilder, P.: Über Störungen der Bewezwischen der "parkinsonistischen" Mikrographie und der cerebellaren Megalographie, Schweiz. Arch.f.Neurol. et Psychiat. 17:270, 1925.
49. Schilder, P.: Über Störungen der Bewegungsbremsung (teleokinetische Störungen) nebst Bemerkungen zur Kleinhirnsymptomatologie, Ztschr.f.d.ges. Neurol.u Psychiat. 47:356, 1919.

Pendulousness of the Legs as a Diagnostic Test

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THE great practical importance of muscle tonus examination for neurologic diagnosis makes it desirable to have a simple and reliable test which can be performed easily in the office.

Physiologists, long interested in measuring muscle tonus, have designed elaborate devices for this purpose, but unfortunately none of these can be used by the physician in his office. He must resort to an old, rather crude method, that of moving the patient's legs and attempting to appraise and compare the resistance he feels. Simultaneous examination of both limbs is impracticable, comparison is difficult, and minimal changes can hardly be detected. The method gives no exact concept of quantitative changes in muscle tonus. If a change in tonus can be demonstrated by this method, other signs or symptoms usually give evidence of the change with much greater clarity.

The simple diagnostic test offered here is more precise. The method described applies only to the lower extremities, but with changes in technique it can also be used in examination for tonus of the upper extremities.

PROCEDURE

The patient sits on the edge of a table with his legs hanging freely. The examiner lifts the patient's legs simultaneously to the same horizontal level, then releases them, permitting them to swing freely. Or the examiner pushes both legs backward, then suddenly removes his hands allowing the legs to swing. The table should not have a crossboard or any other construction which might interfere with the free swinging of the legs.

Unhindered, involuntary, completely automatic swinging is the basic essential for correct performance of this test. The patient must not interfere in any way with the free swinging, though this is sometimes very difficult to achieve. If the examiner says, "Let your legs swing," the patient

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may move them voluntarily; if, "Do not move your legs yourself," he may hold them stiff. The examiner should try to divert the patient's attention and make him relax the legs completely. The tenseness with which some patients hold their extremities is often amazing. It may be difficult and require much time for them to relax. Occasionally, relaxation simply cannot be achieved, in which case the test cannot be used. Interestingly, the hemiplegic patient is apt to interfere with the pendulous movement of the unaffected leg much more than with that of the affected side.

There is a characteristic precision and regularity in the motion of normal free-swinging limbs. The range of successive movements diminishes steadily and evenly, and therefore, it is easy to detect any voluntary interference with swinging of the legs. If the patient interferes either by exaggerating a swing or by impeding it, it is obvious immediately that the resultant movement is actively produced, and it can easily be distinguished from any pattern of movement occurring in normal or pathologic conditions.

In the normal person, the legs usually swing six or seven times after displacement. There is no apparent relation between the range of the displacement and the number of swings. If one leg swings longer than the other, the presence of some abnormality must be assumed. In order to ascertain this difference, the test must be repeated several times.

After the swinging *time* has been determined, the swinging *quality* should be appraised. Normally movements are smooth and regular. Abnormalities are observed usually in the forward swing which may be more accentuated due to a jerky movement of greater range. On the backward movement, the heel does not swing back as far as in the normal; this occurs when the tonus of the extensor muscles of the knee is greater than that of the flexors, as in spastic paralysis.

It is also important to watch whether the leg swings in a strictly anteroposterior plane—a vertical plane perpendicular to the swinging axis. It may not; the pattern of movement of the tip of the foot may be zigzag, a flattened ellipse, a diagonal, an irregular circle or any combination of these, instead of a straight line.

APPLICATIONS IN DIAGNOSIS

The most striking abnormality in pendulousness of the legs is found in such diseases as paralysis agitans and postencephalitic parkinsonism. No other condition influences it to such a degree as extrapyramidal rigidity. The swinging time is markedly diminished, but changes are quantitative only. There are no obvious qualitative variations. In advanced cases of

parkinsonism, although the patient may still be ambulatory, the legs may not swing at all or they may swing only once or twice.

This test is valuable in the diagnosis of unilateral parkinsonism. For example, a patient with mild signs and symptoms of incipient parkinsonism involving the left arm denies on interrogation that his left leg is in any way affected. On routine examination, only minimal or questionable abnormality of the left leg is found, but the test for pendulousness reveals that swinging of the left leg is markedly diminished. Thus, in a case of parkinsonism in which involvement of only the left upper extremity is clinically evident, simultaneous involvement of the lower left extremity can be detected by this test.

Another illustrative case is that of a patient with the usual signs and symptoms of unilateral parkinsonism who thinks that only one side is involved. On examination, the only definitely pathologic sign on the other side is diminution of the swinging time of the leg. The great value of this test in diagnosis of incipient extrapyramidal rigidity seems incontestable.

Spasticity due to pyramidal lesions does not influence pendulousness as much as does rigidity due to extrapyramidal lesions. It is not uncommon to find all the signs of a pyramidal lesion in the lower limbs and the pendulousness little affected, except for some jerkiness in the forward movement. If there is any change, it lies more in quality than in quantity. In pyramidal spasticity, movements are jerky and irregular, the forward movements are brisker than the backward, and the range of backward movement is diminished. The most outstanding characteristic, however, is that the limb does not swing in a precise anteroposterior plane. Movements are zigzag; the tip of the foot describes irregular patterns such as a flattened ellipse, a broken circle, a spiral or an undefinable figure. It is sometimes possible to detect spastic hemiparesis on the basis of this test alone.

In bilateral spastic paralysis, though the usual clinical signs and symptoms are the same on both sides, there still may be a qualitative and quantitative difference in the pendulousness of the lower limbs. This is difficult to explain on purely clinical grounds.

Thus far only muscular hypertonia has been considered. It has been found that the extrapyramidal type (rigidity) mainly influences the quantity of the pendulous movements, and the pyramidal type (spasticity) mainly the quality. In contrast, hypotonia of any origin influences the quantity of movement; the overall swinging time of the affected leg is longer. This occurs in affections of the cerebellum and of its connections. If there is a lesion of both the cerebellum and the pyramidal systems, as in so-called pseudotabetic multiple sclerosis, the cerebellar influence

usually predominates and pendulousness is increased. This increase occurs also in any involvement of the lower motor neuron, such as poliomyelitis, progressive spinal atrophy, spinal cord tumor, prolapse of an intervertebral disc, postanesthetic spinal syndrome with radiculitis in the lumbar region, neuritis of the cauda equina, femoral neuritis, muscular dystrophy and arthrogenic muscular atrophy (after knee injury). In all these conditions, if the affection is unilateral, the leg on the involved side swings strikingly longer. If it is bilateral, the increase in pendulousness parallels the severity of the lesion.

Occasionally, slight abnormalities of pendulousness appear simply as isolated phenomena. A diagnosis cannot be based on this test alone, of course, but that holds true of every test in neurology. Abnormal pendulousness of the legs may be diagnostically decisive, however, if it fits into the whole clinical picture. Its importance lies chiefly in alerting the examiner and in focusing his attention on possible early organic disturbances, thus leading to further corroborative investigations. The thought-provoking property of this simple test is of particular clinical value.

Reviewing personal experiences with this test over many years, it must be stated that: (1) It is sometimes impossible to get the patient to relax sufficiently to allow for correct performance of the test. (2) It is sometimes difficult to evaluate the significance of the observed abnormalities. (3) This test brings up many questions that cannot yet be answered. Generally speaking, however, this simple test has been found to be of definite, practical diagnostic value. It deserves to be used routinely in everyday neurologic examination.

It must be emphasized that pendulousness of the legs in this test should be studied as it occurs after passive displacement, not after tapping the patellar tendon in elicitation of the quadriceps reflex.

"Pendular reflex" is a very familiar term. Marburg[1] attributes this term to Gordon Holmes,[2] but it is generally attributed to André-Thomas,[3] who used it in 1914. However, Van Gehuchten[4] spoke of a "pendular reflex of the leg" in an article in 1908 on tendon reflexes. André-Thomas[3] observed, in a case of left-sided cerebellopontine angle tumor, that the left leg performed a series of oscillations consisting of extension and flexion on tapping the patellar tendon. In his fundamental work on the cerebellum, Gordon Holmes[2] repeatedly referred to the patellar reflex in cerebellar injury. He said of the patellar reflex, ". . . while the normal limb falls deliberately to its original position and quickly comes to rest, that of the affected side often continues to swing inertly to and fro for a time like a pendulum; the jerk has consequently the pendular character described by André-Thomas." He spoke of a "pendular jerk" and of "the pendular

knee jerk of cerebellar disease." Descomps, Merle and Quercy[5] also described pendular reflexes in cerebellar affections. Most of the work published since on this subject has dealt with cases of cerebellar dysfunction. Here the diminution of muscle tonus permits increased pendulousness of the legs after the patellar reflex is elicited.

In their work on olivopontocerebellar atrophy in 1948, Critchley and Greenfield[6] spoke of "pendular knee jerks" as the chief manifestation of that cerebellar disorder. De Nigris[7] reported pendular knee jerk, not in cerebellar, but in frontal lobe hypotonia. Some authors investigated the patellar pendular reflex in pyramidal lesions (Van Gehuchten;[4] Foix and Marie;[8] Heymanowitsch;[9] Austregesilo, Costa-Rodrigues and Marques;[10] Maikov and Kunicyn[11]). Van Gehuchten[4] studied the pendulousness of the legs in spastic paraplegia, not by elicitation of the patellar reflex, but by displacement of the lower leg. However, he still used the term "réflexe pendulaire de la jambe" and regarded his article as a "contribution to the study of the tendon reflexes." Foix and Marie[8] spoke of "hypertonic pendular reflex," Maikov and Kunicyn[11] of "rhythmic hypertonic knee reflex," Austregesilo et al.,[10] of "pseudopendular" or "oscillatory" hypertonic reflex. Alajouanine, Thurel and Fauvert[12] distinguished an "oscillatory hypertonic reflex" of Foix and Marie and a "pendular reflex" of André-Thomas. Benedek and de Thurzo[13] and von Bagothay[14] studied the "pendular patellar reflex" in the cerebellar form of multiple sclerosis. Maikov[15] investigated the behavior of André-Thomas' pendular reflex in normal persons. In the fundamental work of André-Thomas on muscle tonus,[16] which summarizes his life work on this problem, there is a chapter on "Réflexes pendulaires."

André-Thomas' term "pendular reflex" found its way into the textbooks in France (Roger, Widal and Teissier[17]) and elsewhere (Wilson,[18] Bing and Haymaker,[19] Nielsen,[20] Brain,[21] and Grinker and Bucy[22]). Wilson,[18] speaking of chorea, said, "Another feature of some cases is a 'pendular' knee jerk of the kind seen in cerebellar hypotonia; despite passive stretch of hamstrings by the shortening quadriceps, their tone is too poor for a 'stretching contraction'; the leg, therefore, swings to and fro like a pendulum." According to Bing and Haymaker,[19] "A reflex peculiar to cerebellar involvement is the pendular knee jerk." Nielsen[20] said: "Pendulum phenomenon of the patellar reflexes is a good sign if positive on one side only. The patient is asked to sit on a table or high surface so that his feet may swing freely after the patellar reflexes are elicited. On the normal side the foot comes to rest after three or four swings, but on the affected side it continues to swing like a pendulum." In discussing "abnormalities of the reflexes" in cerebellar lesions, Brain[21] said, "The tendon reflexes . . . often

exhibit a characteristic change, which is best seen in the 'pendular' knee jerk. The knee jerk is followed by a series of oscillations of the leg. . . ." Grinker and Bucy[22] speak of "pendular patellar reflexes" and "an excessive pendular movement of the patellar reflex."

Clinical descriptions of cerebellar lesions usually contain the statement that the knee jerk was pendulous. According to Keschner and Grossman,[23] "pendulous knee jerks" occur in patients with marked hypotonia, and Grant, Webster and Weinberger[24] observed in their cases of cerebellar tumors "a pendulous tendon reflex." One must object strongly to the use of this term, because the pendular movement of the leg after elicitation of the patellar reflex is not an integral part of this reflex. This was emphasized by Alajouanine, Thurel and Fauvert.[12] Pendulousness of the legs has nothing to do with the reflex as such. It results only from displacement of the leg caused by contraction of the quadriceps muscle. This displacement can be achieved more easily and better merely by passive lifting of the legs to the same horizontal level, an important prerequisite for the exact performance of this test. It cannot be achieved with the same precision by elicitation of the patellar reflex, because it is difficult to tap both patellas with the same force and the strength of the reflex may be different on both sides. Pendulousness should not be called a reflex; it is simply a by-product of it.

The discrepancy between the patellar reflex and the pendulousness test is plainly demonstrated in cerebellar affections. Here there is no parallel between the muscle tonus as indicated by pendulousness and the strength of the reflexes. In cerebellar affections reported by Keschner and Grossman,[23] "the hypotonia was in some cases associated with hyperactive reflexes, in others with decreased reflexes and in still others with absent deep reflexes." The difference is further demonstrated in mild pyramidal lesions when the quadriceps reflex may be markedly increased, but the pendulousness not appreciably altered.

The arbitrary association of pendulousness of the legs with the quadriceps reflex has hindered the practical application of this test and has confused the issue.

REFERENCES

1. Marburg, O., in Alexander, G., and Marburg, O.: Handbuch der Neurologie des Ohres, Berlin, Urban & Schwartzenberg, 1926, vol. 3, p. 99.
2. Holmes, Gordon: The symptoms of acute cerebellar injuries due to gunshot wounds, Brain 40:461, 1917; Clinical symptons of cerebellar disease and their interpretation, Lancet 1:1177, 1922; The cerebellum of man, Brain 62:1, 1939.
3. André-Thomas: La fonction des antagonistes dans les mouvements volontaires, passifs, réflexes, chez deux malades atteintes de tumeur de la fosse cérébrale postérieure, intéressant le cervelet ou les voies cérébelleuses. Réflexes pendulaires, Rev. neurol. 28:111, 1914.
4. Van Gehuchten, A.: Le mouvement pen-

dulaire ou réflexe pendulaire de la jambe. Contribution à l'étude des réflexes tendineux, Nevraxe 10:261, 1908.

5. Descomps, P.; Merle, P., and Quercy: Syndrome cérébelleux dissocié; Hypotonie. Réflexes pendulaires. Rotation sur l'axe longitudinal. Intégrité des mouvements volontaires, Rev. neurol. 35:222, 1919.
6. Critchley, M., and Greenfield, J. G.: Olivo-ponto-cerebellar atrophy, Brain, 81: 343, 1948.
7. De Nigris, G.: Sui disturbi dell'equilibrio e della coordinazione motoria nelle lesioni dei lobi prefrontali, Arch. gen. di neurol. psichiat. e psicoanal. 14:302, 1933.
8. Foix, C., and Marie, J.: Réflexe pendulaire hypertonique, Rev. neurol. 1:58, 1926.
9. Heymanowitsch, A. J.: Die ampholaterale Pendelmodifikation des Kniereflexes, Deutsche Ztschr. f. Nervenh. 93:119, 1926.
10. Austregesilo; Costa-Rodrigues, and Marques, A.: Les réflexes pendulaires et pseudo-pendulaires, Rev. neurol. 2:262, 1927.
11. Maikov, S., and Kunicyn, V.: On the rhythmic hypertonic knee reflex, Sovrem. psikhonevrol. 9:677, 1929.
12. Alajouanine, T.; Thurel, R., and Fauvert, R.: Nouvelle contribution à l'étude du réflexe oscillatoire hypertonique, Rev. neurol. 2:96, 1934.
13. Benedek, L., and de Thurzo, E.: Sur un cas de forme pendulaire aux axes multiples du réflexe rotulien, Rev. neurol. 2:703, 1930.
14. von Bagothay, L.: Beitrag zu den Entstehungsbedingungen des pendelnden Kniereflexes im Zusammenhang mit einem Falle von multipler Sklerose, Montschr. f. Psychiat. u. Neurol. 92:40, 1935.
15. Maikov, S.: The phenomenon of pendular movement in the normal knee joint, Obozr. psikhiat., nevrol. 4:275, 1929.
16. André-Thomas, and de Ajuriaguerra, J.: Étude Sémiologique du Tonus Musculaire, Paris, Éd. Méd. Flammarion, 1949, p. 507.
17. Roger, G. H.; Widal, F., and Teissier, P. J.: Nouveau Traité de Médecine, Paris, Masson et Cie., 1928, vol. 18, p. 569.
18. Wilson, S. A. K.: Neurology, London, E. Arnold and Co., 1940, p. 614.
19. Bing, R., and Haymaker, W.: Textbook of Nervous Diseases, ed. 5, St. Louis, C. V. Mosby Company, 1939, p. 560.
20. Nielsen, J. M.: A Textbook of Clinical Neurology, ed. 2, New York, Paul B. Hoeber, Inc., 1946, p. 173.
21. Brain, W. R.: Diseases of the Nervous System, ed. 3, New York, Oxford University Press, 1947, p. 51.
22. Grinker, R. R., and Bucy, P. C.: Neurology, ed. 4, Springfield, Illinois, Charles C Thomas, 1949, p. 20, 36, 273, 311, 324, 328.
23. Keschner, M., and Grossman, M.: Cerebellar symptomatology evaluation on the basis of intracerebellar and extracerebellar lesions, Arch. Neurol. & Psychiat. 19:78, 1928.
24. Grant, F. C.; Webster, J. E., and Weinberger, L. M.: Unusual symptomatology with tumors of the cerebellum based on 158 verified cases, Am. J. M. Sc. 202:313, 1941.

Neurility and Neural Excitants

● Every stimulus capable of acting on a nerve causes in it the development of the nervous force, the true nature of which is extremely problematical. For a long time there has been a decided tendency to regard this force as some form of manifestation of electricity; but just in proportion as we have come to know more of the true relations of the latter force to nerve tissues has the probability of the identity of nerve force and electric force diminished.

Beyond a doubt, certain electrical phenomena exist in connection with all nerves and in the presence of all nerve action; but so far from these facts showing that nerve force is electricity, their whole bearing is to prove quite the contrary.

—S. Weir Mitchell in *Injuries of Nerves and Their Consequences*, published in 1872.

The Electroencephalogram in Intracranial Aneurysms

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INTEREST in vascular lesions of the intracranial contents has greatly increased in recent years. Pathologic and angiographic studies have shown that most spontaneous intracranial hemorrhages are secondary to rupture of congenital aneurysms. Although there is great variance in the statistics cited by many authors, the fact remains that the mortality from ruptured aneurysms is high. Furthermore, with repeated ruptures, mortality and morbidity increase.

Only within the past few years has any rational surgical approach been made to these lesions. Evacuation of intracerebral hematomas and ligation of the carotid arteries in the neck are, for the most part, palliative procedures. Studies of the arterial blood flow of the circle of Willis have shown that ligation of the carotid arteries may be effectual only when the aneurysm is located on the internal carotid artery. When the aneurysm is situated elsewhere in the circle, carotid ligation may even be detrimental. Thus, hemiplegia is a not infrequent complication of this procedure, irrespective of preliminary prophylactic progressive compression of the carotid arteries in the neck. The hemiplegias may occur immediately or be delayed days to weeks, and may be temporary or permanent. Thus it would seem desirable to develop a procedure aimed at cure of the defect in the vascular system, e.g., trapping of the aneurysm and excluding it from the cerebral circulation.

However, a major problem from the surgical standpoint is the difficulty frequently encountered not only in localization but also lateralization of the aneurysm. Even after rupture many aneurysms demonstrate no focal clinical symptoms or signs. Furthermore, some fail to be demonstrated by arteriography. Injection of an opaque medium into the internal carotid vessels demonstrates, at best, the anterior and middle cerebral

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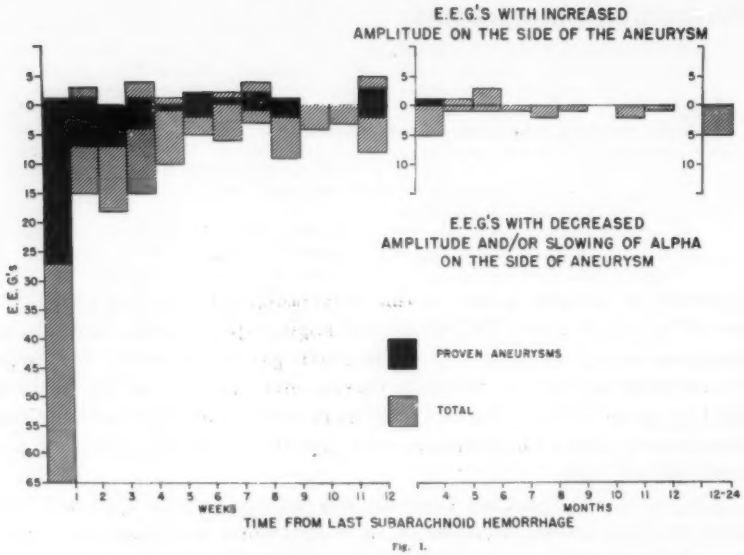


Fig. 1.

FIG. 1. Demonstration of the temporal relationship of amplitude asymmetry to rupture of aneurysms. It will be noted that within the first week subsequent to rupture there is almost uniform ipsilateral amplitude reduction. In subsequent weeks the asymmetry may fluctuate. The end result, which is usually seen after three months, is uniform ipsilateral amplitude reduction.

group. Rarely are the posterior arteries shown. Vertebral artery injection, which may demonstrate the latter vessels, has not as yet been perfected for routine use. Hence, if these lesions are to be attacked surgically, it is desirable to develop some procedure which would at least uniformly lateralize the aneurysm. The electroencephalogram, when used serially, would seem to lend itself readily to such study.

Our interest in these lesions has been aroused because of the relatively large number encountered. Opportunities to study them from an electroencephalographic, angiographic, surgical and postmortem standpoint has led to interesting correlations. A total of 95 aneurysms are reported, of which 42 were proven by arteriography or operation or by autopsy examination. The prime considerations in this study are the correlative electroencephalographic findings and include attempts at: (1) lateralization, (2) localization, (3) study of phenomena associated with rupture, e.g., vasospasm, thrombosis, (4) effect of ligation of the carotid arteries in the neck, (5) effect of direct surgical attack on the aneurysm, (6) dynamic serial studies and (7) end results.

METHODS

For the most part, electroencephalograms were made with an eight channel Grass ink-writing electroencephalograph. At least twelve electrodes were applied, ten to the scalp and one to each ear. The scalp electrodes were placed in the usual frontal, parietal, occipital, and anterior and posterior temporal sites. Recordings were taken with the scalp electrodes referred to both ears, to the ipsilateral ear, to the contralateral ear and to each other. Most electroencephalograms were taken using needle electrodes. Sleep records, either spontaneous or induced, were obtained in some cases.

Arteriograms were done in most cases percutaneously. A few were carried out by the open method. An aqueous solution of 35 per cent Diodrast was used for the most part, and several times Thorotrast was employed. Ten ml. of the solution were given at each injection. At least four injections were made, two in the anteroposterior and two in the lateral positions, and attempts were directed toward obtaining stereoscopic views. Arteriography or intracranial trapping was performed on the side indicated by the electroencephalogram. In two cases operation was performed as indicated by electroencephalographic lateralization in spite of negative bilateral arteriograms and absence of focal symptoms and signs.

RESULTS AND DISCUSSION

Of the 95 cases reported, 42 had aneurysms as demonstrated by arteriography, operation or autopsy. Four of these gave no history of rupture (figures 5 and 9). One of these four bled subsequently. In the remaining cases the clinical picture was similar to the proved aneurysms and included a history of an ictal onset with severe vertical, suboccipital and posterior cervical headache, focal neurological signs (hemiparesis or cranial nerve palsies), and bloody cerebrospinal fluid. The electroencephalographic picture was similar in both groups.

A total of 264 electroencephalograms were taken. Particular attention was paid to: (1) delta activity, (2) amplitude changes (background activity exclusive of slow waves), (3) slowing of the alpha activity and (4) depression of sleep spindles. In all cases attempts were made to localize as well as lateralize these four types of disturbances. In most instances serial records were obtained, varying from days to months, and taken with particular reference to any change in the patient's condition or an intercurrent surgical procedure. Amplitude asymmetry was notable especially in the temporal and occipital areas. Delta foci, when present, were most commonly seen in the temporal and frontal regions. Slowing of the

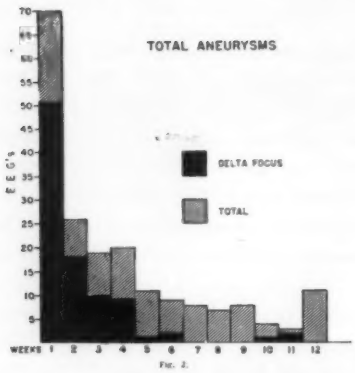
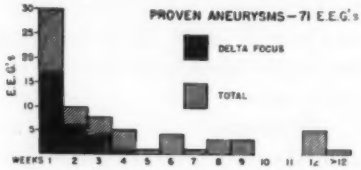


FIG. 2. Showing high incidence of ipsilateral delta foci in first week subsequent to rupture of an aneurysm. Persistence of such foci after the first week and certainly after the third week usually implies an associated intracerebral hematoma, repeated bleeding or thrombosis. These foci are usually associated with aneurysms of the middle and anterior cerebral and anterior communicating arteries.



alpha could be detected best in the posterior temporal and occipital areas.

The presence of these crucial changes in the electroencephalogram would appear to depend on: (1) temporal relationship to rupture, (2) presence of an intracerebral hematoma, (3) associated phenomena such as thrombosis or vasospasm, (4) patency of the vascular bed following such procedures as carotid ligation or intracranial trapping of the aneurysm and (5) the site of the aneurysm.

Serial changes in the electroencephalogram subsequent to rupture of an aneurysm (figures 1 and 2). Sixteen of the 42 proven aneurysms, or 42 of the total 95 proved or presumptive cases, had electroencephalograms within the first week subsequent to rupture. In many instances electrograms were done repetitively in the first week, a total of 73 electroencephalograms. Of those done within the first week, 46 showed a decrease in amplitude plus a slow wave focus; 17 showed a decrease in amplitude alone; seven showed a slow wave focus alone; one showed only slowing of the alpha activity; one had slowing of alpha plus increase in amplitude; and, finally, one showed slowing of alpha plus an increase in amplitude and a slow wave focus. All of these phenomena were noted on the side of the aneurysm.

Thus, the most common finding in the first week was an ipsilateral decrease in amplitude with or without delta activity, as shown in 63 of the 73 electroencephalograms (figures 3, 4, 5 and 7). In the absence of amplitude asymmetry, an ipsilateral slow wave focus alone was the next most common finding, evidenced in six electroencephalograms (figures 4 and 5). However, if the amplitude is increased, with or without delta activity, slowing of the alpha on the side of the aneurysm is important, as seen in two electroencephalograms. In one instance ipsilateral slow-

ing of the alpha was the only notable sign. During sleep the fourteen per second spindles are reduced on the side of the aneurysm.

Focal delta activity rapidly disappears after the first week. Usually its persistence after the third week indicates one or a combination of the following factors: (a) intracerebral hematoma (figure 8), (b) additional bleeding (figure 5), (c) thrombosis and (d) surgical interference such

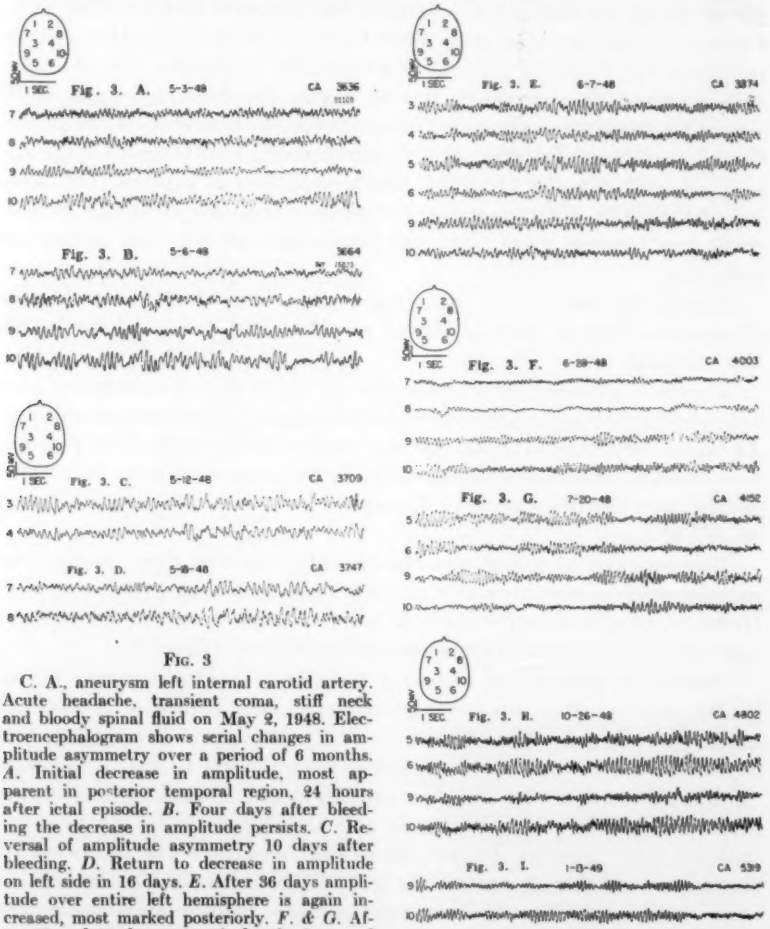


FIG. 3

C. A., aneurysm left internal carotid artery. Acute headache, transient coma, stiff neck and bloody spinal fluid on May 2, 1948. Electroencephalogram shows serial changes in amplitude asymmetry over a period of 6 months. *A*. Initial decrease in amplitude, most apparent in posterior temporal region, 24 hours after ictal episode. *B*. Four days after bleeding the decrease in amplitude persists. *C*. Reversal of amplitude asymmetry 10 days after bleeding. *D*. Return to decrease in amplitude on left side in 16 days. *E*. After 36 days amplitude over entire left hemisphere is again increased, most marked posteriorly. *F*. & *G*. After 57 and 79 days respectively, the increased amplitude is still present on the left. *H*. & *I*. One hundred seventy-seven and 256 days subsequent to rupture of the aneurysm there is a marked reduction in amplitude on the left side, most notable in the posterior temporal region. This is the permanent amplitude reduction which usually is apparent by the third month following rupture.

as carotid ligation or intracranial trapping of the aneurysm (figures 4, 6 and 8).

Although ipsilateral decrease in amplitude is the most common initial finding subsequent to rupture of an aneurysm, the asymmetry may vary in the following weeks to months. Thus, for example, it is not uncommon to see an ipsilateral decrease in amplitude lasting from 10 to 21 days replaced by an increase in the voltage in the temporal and occipital areas, lasting a similar period of time. Then there is a return to another voltage reduction which usually persists, or a repetition of another cycle of amplitude increase, then decrease. In any event, the final end stage in all surviving aneurysms, surgically treated or not, is ipsilateral voltage reduction of a substantial degree, 50 per cent or more. This terminal stage appears in most cases by the third month after the last rupture. The slowing of the alpha activity does not disappear until the electroencephalogram has become stable, i.e., the appearance of the final amplitude reduction.

There were four proved aneurysms in this series which had no history of rupture. Three showed ipsilateral amplitude reduction and the fourth was increased.

Presence of intracerebral hematoma. Of the 42 proved aneurysms, nine had intracerebral hematomas demonstrated either at operation or autopsy. All had a very marked ipsilateral slow wave (delta) focus. Two patients were followed electroencephalographically for a period of more than three months and the delta activity disappeared after an interval of between 80 and 90 days.

The presence of a slow wave focus within the first three weeks after rupture of an aneurysm may or may not suggest an associated hematoma. However, persistence of a delta focus after three weeks would seem to indicate the presence of an intracerebral hematoma (figure 8).

Associated phenomena, including thrombosis and/or vasospasm. Following rupture of an intracerebral aneurysm hemiparesis of a transient nature is frequently seen. This may last from several hours to several days. In these instances, slow activity, contralateral to the hemiparesis (ipsilateral to the aneurysm), is invariably noted. This delta focus rarely persists longer than the hemiparesis, and probably indicates spasm of the vascular tree (figure 5). In two proved instances there was an associated thrombosis and they showed a slow wave focus which persisted or became worse until death. The electroencephalographic picture in the latter was impossible to differentiate from an intracerebral hematoma (figure 4).

Patency of the vascular bed following such procedures as carotid ligation in the neck and/or intracranial trapping of the aneurysm. Ten of the

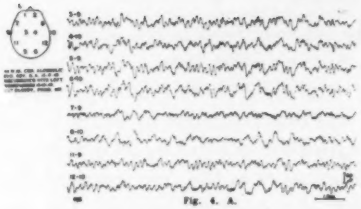


Fig. 4. A.

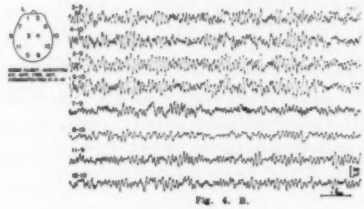


Fig. 4. B.

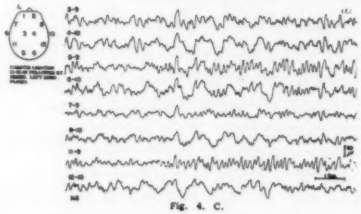


Fig. 4. C.

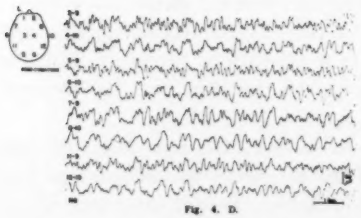


Fig. 4. D.

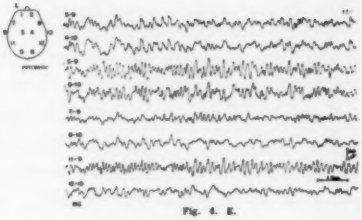
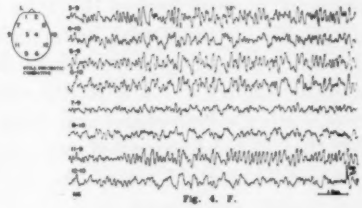


Fig. 4. E.



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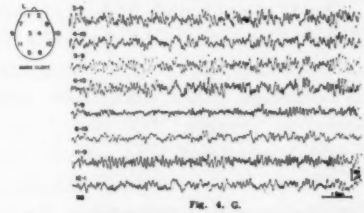

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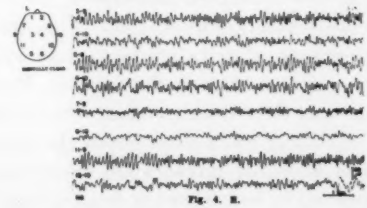


Fig. 4. H.

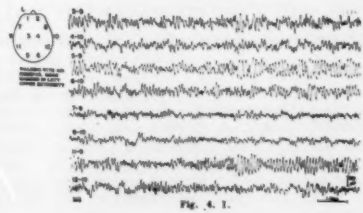


Fig. 4. I.

FIG. 4

J. H., aneurysm right anterior cerebral artery. (1) Initial delta activity usually seen associated with rupture of aneurysm of the middle cerebral, anterior cerebral or anterior communicating arteries; (2) resolution of delta activity; (3) effect on electroencephalogram of carotid ligation in neck, with resultant immediate, persistent contralateral hemiparesis; (4) subsequent serial changes in electroencephalogram with particular reference to resolution of delta activity.

A. Three days subsequent to rupture moderate delta activity on right side, most marked in temporal areas; also decrease in background activity on right side. *B.* Resolution of delta activity, concomitant with improvement in hemiparesis, by 13th day subsequent to rupture. Amplitude in right temporal area still decreased. *C.* Two days subsequent to right carotid ligation in neck. Marked delta activity with reduction in voltage of background activity on entire right side; 24 hours later slow activity is worse and more generalized (D) (? cerebral edema). Delta activity gradually resolves over the next two months after ligation. *C, D, E, F, G, H & I.* Persistent reduction in amplitude on entire right side for at least three months subsequent to ligation of carotid vessels in neck.

42 proved aneurysms had ligation of the internal carotid or common and external carotid arteries in the neck. In five instances there was no resultant hemiparesis. In two cases there was immediate contralateral paralysis, and in the remaining three hemiplegia was delayed from 24 hours to ten days. In five cases which successfully withstood carotid ligation without clinical complications, there were no slow waves in the electroencephalogram or no increase of the delta activity, if previously present. The appearance or worsening of the delta activity subsequent to carotid ligation invariably accompanied hemiplegia. In three of the hemiplegic cases, disability was permanent and the delta activity persisted for almost three months (figure 4). The fourth died 23 days after ligation. In the fifth case, both the hemiplegia and delta activity remained for two weeks. It is felt that in the former instances, there was thrombosis of a part or all of the middle cerebral artery, and in the latter the pathophysiologic change was mainly vasospasm.

In 17 cases which had intracranial trapping of their aneurysms, three died and two others developed hemiplegia. Of the 12 which survived without sequelae, there was no change in the electroencephalogram subsequent to operation other than those which would be expected secondary to operative trauma. The two cases which developed hemiplegia showed marked ipsilateral delta activity following operation.

Hence, if the cerebral vascular bed is left patent following either of the two operative procedures, there will be no resultant clinical or electroencephalographic changes. Alterations in the electroencephalogram (appearance of delta activity) following these operations probably indicate vasospasm and/or thrombosis. Persistence of the slow activity beyond several days usually means the latter.

Site of aneurysm. From the data listed above, it is felt then that one can lateralize intracranial aneurysms. Thus far however, localization has proved to be somewhat frustrating. Nevertheless, there is some indication that with wider experience this goal may be attainable. Distribution of the 42 proved aneurysms is shown in table 1.

TABLE I
DISTRIBUTION OF INTRACRANIAL ANEURYSMS

Internal Carotid	*Middle Cerebral*	*Anterior Cerebral*	*Anterior Communicating*	*Posterior Communicating*
18	11	5*	4	4

*One aneurysm was located at the bifurcation of the anterior cerebral and anterior communicating arteries.

Electroencephalographic studies in this group have shown that delta foci are rarely seen following rupture of aneurysms of the internal carotid (figures 3 and 7) and posterior communicating arteries. In the initial

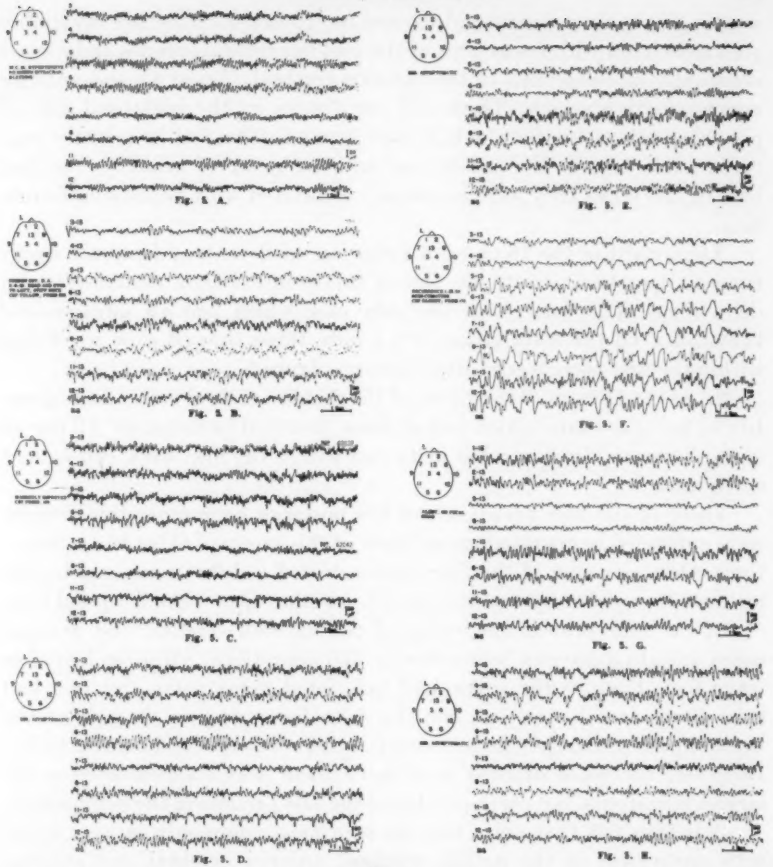


FIG. 5.

A. M., aneurysm of right internal carotid artery. Initial electroencephalograms taken 20 months prior to any known rupture. Serial recordings show changes in amplitude and delta foci subsequent to two separate ruptures of the aneurysm. If focal delta activity is present subsequent to rupture of internal carotid artery, this usually resolves rapidly.

A. Electroencephalogram of unruptured aneurysm. No history of previous bleeding. Amplitude in right temporal region reduced, marked posteriorly. *B*. Twelve days after acute ictal episode with headache, conjugate deviation of head and eyes to left, left hemiparesis and bloody cerebrospinal fluid. Amplitude is decreased on entire right side, marked posteriorly. Some delta activity still apparent in right temporal area. *C*. Twenty-six days after initial rupture delta activity has disappeared and amplitude in right posterior temporal region is increasing. *D*. Increased amplitude in right posterior temporal and occipital areas is marked 37 days after rupture. *E*. Fifty-eight days after rupture the amplitude over entire right side is tending to decrease. *F*. Three days following second rupture the recording shows generalized delta activity, more marked on right side with decrease in background activity on that side. *G*. Five days after second rupture the electroencephalogram already shows resolution of slow activity with definite reduction in amplitude on right side, marked in temporal areas. *H*. Eleven days after second rupture the recording already shows tendency to reversal of amplitude asymmetry. Increased amplitude is apparent in the ipsilateral posterior temporal and occipital areas.

weeks (one to three weeks) subsequent to rupture, such foci are invariably seen associated with aneurysms of the middle cerebral arteries and almost constantly in aneurysms of the anterior cerebral (figure 4) and anterior communicating vessels. These foci are always on the ipsilateral side. A possible explanation for the high incidence of delta foci in recently ruptured aneurysms of the middle and anterior group of vessels is the fact that in this series they were commonly associated with hematoma formation.

Thus, eight of the 18 cases of aneurysm of the internal carotid artery came to operation or autopsy. One of this group of eight demonstrated a delta focus. This latter was the only case which had an intracerebral hematoma. Of the total group of 18, only three showed slow wave foci within the first three weeks after rupture (figure 5).

Six of the 11 cases of aneurysm of the middle cerebral artery had operative or autopsy examination and of these, four had hematomas. All eleven cases, however, demonstrated delta foci within the first week subsequent to rupture.

Three of the four aneurysms of the posterior communicating arteries were autopsied or operated upon. None of this group of three had a hematoma. Only one case of the four demonstrated a delta focus, and in this instance there was an associated ipsilateral infarction of the temporal lobe.

Of the nine proved aneurysms of the anterior cerebral and anterior communicating arteries, seven died or had operations. All seven had slow wave foci. Four of the seven had associated hematomas and two had infarctions. In all cases but one the delta focus was on the side of the hematoma or infarction. In one instance there was bilateral delta activity. However, the more marked slow wave focus was contralateral to the largest hematoma, but corresponded to the side producing the hemiparesis.

It is thus felt that delta foci are seen most commonly in association with aneurysms of the middle cerebral, anterior cerebral and anterior communicating arteries, with or without intracerebral hematoma. However, in this group of cases, bleeding within the substance of the brain appears most likely with aneurysms in these sites. More proved cases will have to be studied before definite conclusions can be made on this point.

CONCLUSIONS

Multiple electroencephalograms were taken on 42 cases of proved aneurysms and in an additional 53 cases of spontaneous subarachnoid hemorrhage with hemiparesis or cranial nerve palsies. Recordings were taken as soon after the history of rupture of the aneurysm as possible, and subsequent serial records were made in many instances. The electro-

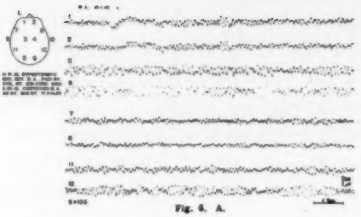


Fig. 6. A.

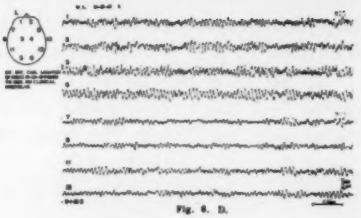


Fig. 6. D.

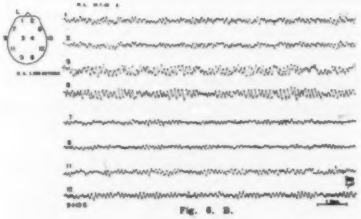


Fig. 6. B.

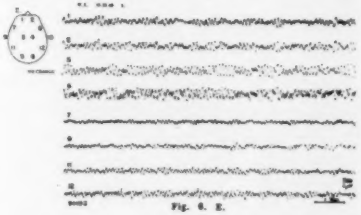
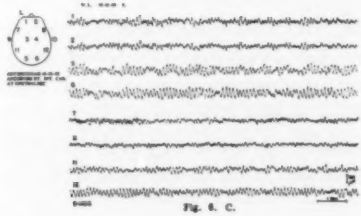


Fig. 6. E.



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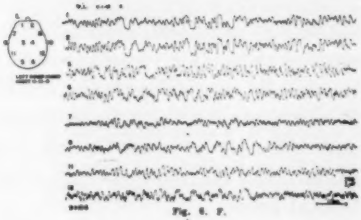

Fig. 6. F.

FIG. 6

W. L., aneurysm right internal carotid artery at the level of the ophthalmic artery. Rupture on Aug. 24, 1949. Ligation of right carotid vessels in the neck on Oct. 20, 1949 with delayed (10 days) hemiplegia and effect on the EEG. Patient died Nov. 12, 1949.

Demonstrates: (1) importance, at times, of obtaining serial recordings when patient is seen later than one week subsequent to rupture of aneurysm; (2) serial changes in amplitude following rupture of an aneurysm; and (3) delayed effects (clinical and electroencephalographic) subsequent to carotid ligation. *A*. Thirty-eight days after rupture there is an increase in amplitude in the right posterior temporal and occipital regions. The right anterior temporal area lags, since the amplitude here is reduced. *B*. Six days after previous recording the amplitude asymmetry is less marked. However, the greatest changes in voltage have occurred on the right side. *C*. Six days later the amplitude in the posterior temporal and occipital areas has again increased. *D. & E.* Although the right internal carotid artery has been ligated in the neck, there is no delta activity in the electroencephalogram and as expected no clinical sequelae. *F*. Ten days after carotid ligation patient developed left hemiplegia. The electroencephalogram taken two days later (twelve days after ligation) shows diffuse delta activity, most marked in the right temporal region.

encephalographic picture in the proved and unproved aneurysms was identical. In four proved aneurysms there was no history of rupture.

In all instances the initial changes in the electroencephalograms within the first one to two weeks subsequent to rupture were: (a) ipsilateral decrease in amplitude, (b) ipsilateral delta focus and (c) ipsilateral slowing of the alpha activity. These three factors were present alone or in combination. Of these the voltage decrease was the most constant factor. With the passage of time, the initial amplitude reduction might be replaced by a subsequent increase, usually in two to four weeks. The end result in all cases, however, was substantial decrease, although the increased phase might reappear one or more times. The permanent voltage reduction usually appeared by the third month subsequent to rupture. The voltage changes were most notable in the temporal and occipital areas. Three of four unruptured aneurysms showed ipsilateral amplitude decrease, the fourth showed increase.

In subsequent weeks following rupture an initial electroencephalogram might appear to be inconclusive for the purpose of lateralization. Serial records taken over the next seven to ten days will usually resolve this difficulty.

Evidence is given that delta foci usually indicate one or more of the following: (a) intracerebral hematoma, (b) vasospasm and/or thrombosis of the major vessel involved in the aneurysm and (c) aneurysm of the middle cerebral, anterior cerebral or anterior communicating arteries. Persistence of a delta focus beyond three weeks subsequent to rupture and without operative interference usually indicates an intracerebral hematoma. The delta foci are most commonly seen in the temporal and frontal areas.

Using the above criteria, the electroencephalogram definitely can lateralize an intracranial aneurysm or hematoma. Although our studies are incomplete, there is some indication that the electroencephalogram may aid in localization.

Five of ten cases treated by carotid ligation in the neck developed immediate or delayed hemiparesis, which was permanent in four cases. In the instances with permanent neurologic sequelae, delta foci remained for three months.

Two intracranial operations for aneurysms were performed only on the basis of electroencephalographic lateralization. A flap was turned down on the correct side, in spite of the absence of focal neurologic symptoms and signs and negative bilateral arteriograms.

Work is now in progress to note changes in the electroencephalogram associated with barbiturate induced sleep and carotid compression.

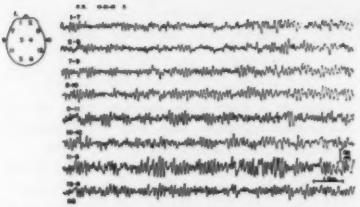

FIG. 7. (*Above*). N. R., aneurysm right internal carotid artery at junction with posterior communicating. Rupture on Nov. 21, 1949, and again Dec. 22, 1949. No focal symptoms or signs. Intracranial trapping of aneurysm on Jan. 12, 1950. No evidence of intracerebral hematoma. Repeated bilateral arteriograms failed to demonstrate aneurysm. Operation was performed on correct side on basis of EEG lateralization alone. Demonstrates: (1) absence of delta focus (aneurysms of internal carotid arteries seldom show delta foci); (2) decrease in amplitude in right temporal region two days subsequent to rupture.

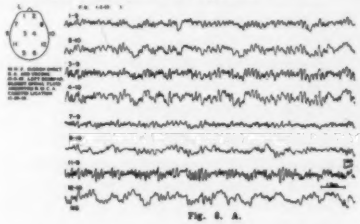

FIG. 8. A.

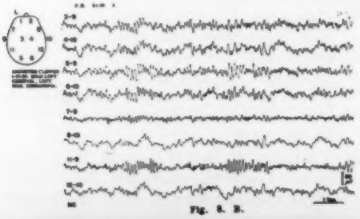

FIG. 8. B.

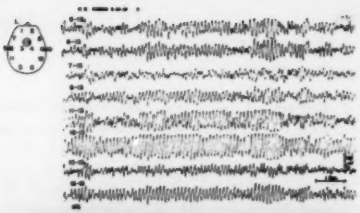

FIG. 9 (*Above*). O. H., large unruptured aneurysm of right internal carotid artery. Incomplete right third nerve palsy for 10 years, complete for 3 weeks prior to electroencaphalogram. EEG: Marked increase in amplitude in right temporal region. In three other unruptured aneurysms the amplitude was decreased on ipsilateral side. (*Lower*) Huge aneurysm outlined by arrows.

FIG. 8 (*Left*). P. H., aneurysm right middle cerebral artery with rupture and intracerebral hematoma on Dec. 8, 1949. Ligation of right carotid vessels in neck on December 20, 1949 and trapping of aneurysm on Jan. 10, 1950. Demonstrates: (1) persistence of delta activity and amplitude reduction frequently seen with ruptured aneurysms of the middle cerebral artery; (2) subsequent to intracranial trapping of aneurysm there was no worsening of either the clinical or electroencephalographic signs. *A*. Presence of delta activity 25 days subsequent to rupture. Persistence of slow activity for such a long period usually indicates presence of an intracerebral hematoma. It is also noted that both the delta activity and amplitude reduction is marked in the temporal regions. *B*. The delta focus and amplitude reduction in the right temporal area is less marked, although intracranial trapping was carried out 22 days prior to the EEG. (*Left*) Arteriogram showing aneurysm right middle cerebral artery.

REFERENCES

1. Chusid, J. G., and deGutierrez-Mahoney, C. G.: Electroencephalographic studies after ligation of the internal carotid artery, J. Neurosurg. 4:86, 1947.
2. Cohn, R.; Raines, G. N.; Mulder, D. W., and Neumann, M. A.: Cerebral vascular lesions (electroencephalographic and neuropathologic correlations), Arch. Neurol. & Psychiat. 60:165, 1948.
3. Cress, C. H., and Gibbs, E. L.: Electroencephalographic asymmetry during sleep (in patients with vascular and traumatic hemiplegia), Dis. Nerv. System 9:327, 1948.
4. Elvidge, A. R., and Feindel, W. H.: Surgical treatment of aneurysm of the anterior cerebral and of the anterior communicating arteries diagnosed by angiography and electroencephalography, J. Neurosurg. 7:13, 1950.
5. Epstein, J. A., and Lennox, M. A.: Electroencephalographic study of experimental cerebrovascular occlusion, EEG & Clin. Neurophysiol. 1:491, 1949.
6. Greenstein, L., and Strauss, H.: The electroencephalogram in subarachnoid hemorrhage, J. Mt. Sinai Hosp. 13:76, 1946.
7. Hurteau, E. F.: Spontaneous subarachnoid hemorrhage, J.A.M.A. 142:988, 1950.
8. Robertson, E. G.: Cerebral lesions due to intracranial aneurysms, Brain 72:150, 1949.
9. Rogers, L.: Carotid ligation for intracranial aneurysms (Report of a case studied by electroencephalography), Brit. J. Surg. 32:309, 1944.
10. Roseman, E., Whitcomb, B. B., and Woodson, F. G.: Carotid sinus syncope secondary to ligation of carotid vessels for intracranial arterio-venous aneurysm (Report of a case with surgical cure, electroencephalographic and electrocardiographic studies), J. Neurosurg. 2:287, 1945.
11. Savitsky, N.; Pacella, B. L., and Stern, F. D.: Electroencephalographic changes in a case of subarachnoid hemorrhage, Arch. Neurol. & Psychiat. 53:232, 1945.
12. Shenkin, H. A.; Harmel, M. H., and Kety, S.: Dynamic anatomy of the cerebral circulation, Arch. Neurol. & Psychiat. 60:240, 1948.
13. Strauss, H., and Greenstein, L.: The electroencephalogram in cerebrovascular disease, Arch. Neurol. & Psychiat. 59:395, 1948.
14. Strauss, H.; Liberson, W. T., and Meltzer, T.: Electroencephalographic studies: Bilateral differences in alpha activity in cases with and without cerebral pathology, J. Mt. Sinai Hosp. 9:957, 1943.
15. Sugar, O.: Asymmetry in occipital electroencephalograms, Dis. Nerv. System 8:141, 1947.
16. Sugar, O., and Gerard, R. W.: Anoxia and brain potential, J. Neurophysiol. 1:558, 1938.
17. Sweet, W. H.; Sarnoff, S. J., and Bakay, L.: A clinical method for recording internal carotid pressure, Surg., Gynec. & Obst. 90:327, 1950.
18. Williams, D., and Reynell, J.: Abnormal suppression of cortical frequencies, Brain 68:123, 1945.
19. Woodhall, B., and Lowenbach, H.: Congenital cerebral aneurysms lateralized by electroencephalography, South. M. J. 36:580, 1943.
20. Yeager, C. L., and Walsh, M. N.: Changes in the electroencephalogram from ligation of the carotid artery, J. A. M. A. 114:1625, 1940.

We wish to thank Dr. Barnes Woodhall and Dr. Guy L. Odom for permission to include their cases which came to surgery.

● The medulla spinalis, which appears like an appendage to the brain, to which it is connected by the medulla oblongata, is seen extending through the vertebral column or bony case, by which it is carefully protected. Connected with the medulla spinalis are thirty-one pairs of nerves. Each of these nerves is attached to the spinal cord by two sets of filaments, or roots, called the anterior and the posterior roots of the spinal nerves.

—Amariah Brigham in *An Inquiry concerning the Diseases and Functions of the Brain, the Spinal Cord and the Nerves*, published in 1840.

Spinal Cord Tumors with Minimal Neurologic Findings

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For several hundred years spinal cord tumors have been known to produce serious neurologic symptoms. It was not until 1888, however, that neurologic localization and surgical technics developed sufficiently to allow Horsley to remove successfully a benign spinal cord tumor which had been correctly diagnosed and localized by Gowers.[1] In those early days surgical treatment of cord tumors was necessarily confined to lesions which produced considerable spinal cord compression, as the diagnosis and localization were dependent on an abundance of neurologic signs. Since then many advances have been made to aid in an earlier diagnosis and more exact localization of spinal cord tumors. The perfection of roentgenologic technics and interpretation has made roentgenograms extremely valuable. The introduction of lumbar puncture as a diagnostic procedure by Quincke in 1891,[2] and the later observations of Froin[3] on xanthochromia and of Queckenstedt[4] and Ayer[5] on spinal fluid dynamics have helped considerably in earlier diagnosis and, in some cases, localization of cord tumors. Finally, the advent of contrast myelography, first with air as proposed by Dandy in 1918[6] and later with iodized oil, as introduced by Sicard and Forestier in 1922,[7] and with Pantopaque by Steinhausen and associates,[8] has made precise localization possible by mechanical means. Thus, at the present time the neurologist is not so much concerned with the localization of cord tumors as he is with early diagnosis and differential diagnosis.

The importance of a knowledge of the early symptoms and signs of spinal cord tumors cannot be overemphasized. Relatively benign tumors can produce irreparable damage to the spinal cord if allowed to progress without proper treatment, and the sequelae greatly belie the benign nature of most of the tumors. Furthermore, cord tumors in certain locations may be present for many years and cause long periods of needless incapacity and suffering. With the modern diagnostic aids and perfected surgical

From the sections on neurology and psychiatry and on neurologic surgery, Mayo Clinic and Mayo Foundation.

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technics, many spinal cord tumors can be demonstrated and removed before serious neurologic deficit occurs. Thus, all physicians should have a high index of suspicion regarding the possible presence of cord tumors.

ANALYSIS OF MATERIAL

In order to review the early symptoms of spinal cord tumors and perhaps to clarify the clinical picture, records of a group of 37 cases of verified spinal cord tumors with minimal neurologic findings have been studied. All cases of protruded intervertebral disk have been excluded from this study because of the high percentage of them that come to operation with essentially negative results of neurologic examination.

The cases under discussion were chosen from a group of 150 cases of tumor of the spinal cord in which operation was performed at the Mayo Clinic during the three-year period from 1946 through 1948. In 32 of the 37 cases there was no evidence of objective neurologic findings at the time of operation. In the remaining 5 cases the results of neurologic examination had been essentially negative at the time of the first examination, but operation was deferred, and by the time the patients came to operation at a later date, definite neurologic changes had developed.

TABLE I
FREQUENCY OF SPINAL CORD TUMORS BY TYPE AND LOCATION

Tumor Type	*Lumbar*	*Thoraco-lumbar*	*Thoracic*	*Cervical*	*Totals*
Neurofibroma	12		2	2	16
Ependymoma	6	4	1		11
Meningioma	1		1		2
Carcinoma	2		1		3
Sarcoma	1			1	2
Lymphoblastoma		1			1
Hemangioma				1	1
Astrocytoma	1				1
TOTALS	23	5	5	4	37

Of the 37 tumors (table 1) 23 were located in the lumbar region, 5 were thoracolumbar, 5 were thoracic and 4 were cervical. The pathologic varieties of tumors consisted of (tables 1 and 3) 16 neurofibromas (14 benign and 2 malignant), 11 ependymomas, 3 metastatic carcinomas, 2 meningiomas, 2 sarcomas (1 neurogenic and 1 angiosarcoma), 1 cavernous hemangioma and 1 lymphoblastoma (Hodgkin's type). The remaining tumor was an ectopic astrocytoma of the cauda equina which will be reported in detail elsewhere. Ten of the tumors were extradural in location, and 27 were found within the dura. The unusually low incidence of menin-

giomas occurring in this series can probably be explained on the basis of two facts: First, the series is hardly large enough to contain a true representation of the pathologic varieties of tumor in the frequencies in which they usually occur; and second, meningiomas are located most frequently in regions where they are likely to produce a neurologic deficit as one of their primary symptoms.

The youngest patient in this series was 11 years of age, and the oldest was 72 years of age. The largest number of patients, 11, was in the sixth decade, and the remaining patients were distributed rather evenly between the second and eighth decades. There were 24 males and 13 females.

TABLE II
FREQUENCY OF SPINAL CORD TUMORS BY LOCATION OF TUMOR AND LOCATION OF PAIN

Location of Tumors	*Location of Pain*									
	Back	*Back and Legs*	*Legs*	*Back and Abdomen*	*Buttocks*	*Shoulder*	*Shoulder and Arm*	*Arm*	*Shoulder and Neck*	*Totals*
Lumbar	1	12	5	2	3					23
Thoracolumbar	1	3			1					5
Thoracic	3	1		1						5
Cervical						1	1	1	1	4
TOTALS	5	16	5	3	4	1	1	1	1	37

It is interesting that pain was the chief complaint of all of the 37 patients. Table 2 gives both the location of the tumor and the location of the associated pain. The onset of pain was gradual in 25 patients and sudden in 12 patients. The pains were variously described as "aching," "cramping," "tingling," "shooting," "burning," "sharp," "stinging," and "radiating." Thirty of the 37 patients complained of severe pain at night or while lying for prolonged periods, and 6 stated that it was so severe that they had to sleep in a semisitting position. All except four of the patients

TABLE III
FREQUENCY OF SPINAL CORD TUMORS BY TYPE AND DURATION OF SYMPTOMS

Tumor Type	*2 mo.*	*3-6 mo.*	*6-12 mo.*	*1-2 yr.*	*2-5 yr.*	*5-10 yr.*	*More than 10 yr.*	*Totals*
Neurofibroma		1	5	1	5	3	1	16
Ependymoma		1	2	2	4		2	11
Meningioma		1		1				2
Carcinoma			3					3
Sarcoma	1		1					2
Lymphoblastoma			1					1
Hemangioma						1		1
Astrocytoma			1					1
TOTALS	1	3	13	4	9	4	3	37

noted an exacerbation of pain on coughing, sneezing or straining, and four patients suffered from extreme constipation because the pain produced by straining prevented them from moving their bowels.

The duration of symptoms (table 3) varied from two months in the case of the neurogenic sarcoma to twenty-seven years in the case of a benign cellular ependymoma. The average duration of symptoms prior to operation was about three and one-half years (42.5 months).

In addition to the chief symptom, 16 patients had associated symptoms of varying types. Five patients complained of a subjective weakness of one or both legs, five complained of numbness, paresthesias or hypesthesia of their legs or feet, one complained of both paresthesias and weakness of the left leg, one complained of fasciculations in his calf muscles, one of weakness of the left arm, one of difficulty in starting his urinary stream, one of abdominal pains and nocturia, and one of a severe progressive scoliosis.

Because 32 of the 37 patients exhibited minimal neurologic changes at the time they came to operation, they will be considered as a group, while the five patients who progressed to a neurologic deficit before operation will be considered independently. Although 32 patients exhibited no diagnostic sensory, motor or reflex disturbance at the time of their operations, certain physical signs were present with sufficient frequency and in sufficient degree to warrant discussion. Twenty-five of the 32 cases exhibited a moderate to marked limitation of spinal motion in the vicinity of the tumor, and 26 patients had definite percussion tenderness in this region. Nineteen patients gave a positive Kernig's or Lasègue's sign or both. Only six patients exhibited a definite scoliosis. A minimal muscular weakness was noted in six patients, but in four of these it was interpreted as being secondary to pain. A slight atrophy was noted in the gluteus muscles in two patients, and in the quadriceps muscle in another. In one case fasciculations were noted in the muscles of one calf, but there was no demonstrable associated weakness of this muscle group. An indefinite sensory disturbance was noted in six of the 32 cases, but in none of them did it follow a dermatome pattern. Twelve patients walked with a limp because of their severe pain, and one was unable to walk. A slight inequality of the knee jerks was found in 12 cases and of the ankle jerks in seven. No patient presented unusually hyperactive reflexes, spasticity or clonus. A diminished anal reflex was found on one occasion, but none of the 32 patients had been incontinent of either urine or feces. One patient having a cervical cord tumor exhibited diminished biceps reflexes bilaterally.

Of these 32 cases, a spinal cord tumor was the suspected diagnosis in 11 instances, and a differential diagnosis between protruded disk and spinal

cord tumor was considered in six others. In eight cases the clinical impression was that of indeterminate intraspinal lesion, and the remaining seven were believed to have protruded intervertebral disks.

As previously noted, five patients were neurologically negative on their first examination, but while under observation and repeated neurologic examinations, definite deficits developed. One of these, a man aged 52 years, was first examined neurologically in 1941 while he was being treated for a severe iritis. A neurologic examination was performed because of an exacerbation of a backache which had been present intermittently for eleven years. Although the results of examination were completely negative, a spinal fluid examination was advised and refused. He returned six years later because urinary incontinence had developed. Neurologic examination revealed little other than a hypesthesia of the saddle area and an absent anal reflex. A myxopapillary ependymoma of the filum terminale measuring 4 by 3 by 2 cm. was removed at operation.

Another case is that of a girl aged 13 years who was first examined in April 1948, at which time she was neurologically negative except for a marked stiffness of her neck. She was suspected of having a cervical cord tumor, but when the spinal fluid examination revealed no evidence of block and a total protein of only 25 mg. per 100 ml., operation was deferred and she was advised to have recheck examinations at monthly intervals. When she returned in May 1948, she exhibited a definite weakness of the left forearm and hypesthesia to pain and temperature in the lower extremities. An intradural, extramedullary neurofibroma was removed from the level of the sixth and seventh cervical vertebrae.

The third case is that of a man aged 56 years who was first seen at the clinic in 1939 with a twenty-year history of intermittent low-back and bilateral leg pain. The results of neurologic examination at that time were completely negative, and conservative treatment was advised. He returned in 1947, at which time he was found to have weakness and atrophy in both legs, markedly diminished knee jerks, and absent ankle jerks. Operation revealed a cellular ependymoma 3 by 2 by 2 cm. involving the cauda equina, which was removed intact.

Another patient, a man aged 48 years came to the clinic in 1943 because he had noted a mass growing in the left side of his neck. His general physical examination revealed little other than the tumor mass. This was excised and proved to be a neurofibroma which extended upward into the foramen between the second and third cervical vertebrae. When the patient had recovered from this operative procedure, he was examined neurologically with negative results. Removal of the intraspinal portion of the dumb-bell tumor was advised but refused. He returned in 1946

because of pain in his neck. Neurologic examination at this time revealed absent abdominal reflexes, unequal cremasteric reflexes and a positive Babinski reflex on the right. An intraspinal removal of the remaining portion of the tumor was accomplished in a two-stage procedure.

The fifth case is that of a woman aged 51 years who came to the clinic in March 1946, complaining of pain in her back and left flank of fifteen years' duration. The results of neurologic examination were negative, but because her spinal fluid protein was elevated, a myelogram with air was carried out. This showed a slight deformity at the interspace between the fourth and fifth lumbar vertebrae. Consequently, a protruded intervertebral disk was removed at this level and, because it was indicated, a spinal fusion was done. The patient returned five months later complaining of severe pain, and after careful examination and an unsuccessful attempt to perform another myelogram, re-exploration of the original operative site was carried out. In spite of the operation, she continued to have pain, and when examined one month later, a saddle hypesthesia was present associated with slight weakness in both legs, hyperactive knee and ankle jerks and a positive left Babinski reflex. The myelogram was repeated with iodized oil, and a tumor was outlined at the level of the eleventh thoracic vertebra. Laminectomy was carried out at this level, and two intradural, extramedullary neurofibromas were found and removed.

TABLE IV
AIDS IN DIAGNOSIS

	Per Cent
Pain (pain on cough or straining or both 90%; night pain 81%)	100
Percussion tenderness over spinal column	70
"Stiff back"	68
Positive Kernig or Lasègue sign or both	57
Subjective complaints	43
Minimal reflex changes	32
Altered gait	32
Positive roentgenographic findings	27
Spinal fluid findings	
Increased protein: more than 50 mg. per 100 ml.	90
Partial or complete block	41
Myelography	90

Roentgenographic examinations of the spinal column were carried out in all 37 cases, and in ten there was evidence of bony changes suggesting an intraspinal tumor. In 15 patients the roentgenograms of the spinal column were negative, in six there were narrowed intervertebral interspaces, in five hypertrophic changes were present and in one case there was evidence of an epiphysitis in the lower thoracic region.

Examinations of the spinal fluid were carried out in 29 instances. In 12 patients a partial or complete spinal fluid block was found. Twenty-six specimens of spinal fluid were observed to have a total protein of more than 50 mg. per 100 ml., the highest estimation being 10,000 mg. per 100 ml. Three specimens were found to have cell counts elevated above five, the highest being 25 white blood cells per cubic millimeter.

Thirty myelograms were performed on 28 patients. Of these, air was used as the contrast medium in four myelograms and either iodized oil or Pantopaque in the remaining 26. The tumors were accurately localized as to level in 27 of the 30 myelograms. The three unsatisfactory myelograms were all performed with air as the contrast medium, and in two cases they were repeated with iodized oil at a later date with satisfactory results.

Forty-four surgical procedures were carried out on the 37 patients. In 27 cases the tumors were removed; in eight instances all visible tumor was extirpated; and in the remaining two patients only biopsy specimens were removed. Thirty-two cases required only one operation, although in one instance exposure through a renal incision as well as a lumbar laminectomy was necessary in order to remove a large dumb-bell neurofibroma. Of the remaining five patients, three required two operative procedures, and two each had three operations. In one instance signs of compression of the cauda equina developed three days after the removal of a neurofibroma, necessitating the evacuation of a postoperative blood clot. In a second case pain developed in the legs after the patient had had twelve months of relief following removal of an ependymoma of the cauda equina. Fourteen months after the original procedure a second operation revealed a large extradural cyst containing cerebrospinal fluid which had compressed the cauda equina. A third patient presented a roentgenographic picture consistent with the diagnosis of giant-cell tumor of the first lumbar vertebra. Consequently, the tumor was removed from this vertebra, and a bone graft was performed by the orthopedic surgeon. When histologic section of the tumor showed that it was a neurofibroma, a laminectomy was performed, and a large extradural extension of the tumor spanning three vertebrae was removed. The two patients that had three operative procedures (of whom one had a dumb-bell neurofibroma of the neck and the other underwent two operations for protrusion of an intervertebral disk and a thoracic laminectomy for removal of two neurofibromas) have been previously described. In addition, one patient in this series of cases had undergone removal of a protruded disk before coming to the clinic.

COMMENT

From the preceding data in 37 cases of spinal cord tumor, several inferences can be drawn which may assist in the earlier diagnosis of these lesions (table 4). The age incidence indicates that cord tumors may occur in any decade of life. The fact that all of the patients complained chiefly of pain should lead one to suspect the possibility of spinal cord tumor in any case in which the patient complains of unremitting pain of unknown origin. The duration of symptoms in this group would tend to indicate that the time element is not of much importance in the differential diagnosis of these lesions. Pain is not always typically radicular, and the location of the pain may be extremely varied from case to case. The onset of symptoms may be gradual or sudden. In many cases, the only complaint may be that of pain. The significance of pain occurring at night or becoming exacerbated while the patient is recumbent should not be overlooked, and the production or increase of pain by acts of coughing, sneezing or straining is also of importance. The fact that in two of the 37 cases operation was performed for protruded disk before the true nature of the lesions was discovered indicates the importance of attempting to rule out spinal cord tumor in cases in which protruded intervertebral disks are suspected. Since routine spinal roentgenograms suggested the presence of a spinal cord tumor in ten of the 37 cases, the value of this examination should be kept in mind. The significance of spinal fluid examination as demonstrated by our series of cases needs no further comment except that a normal spinal fluid protein does not necessarily rule out the presence of a spinal cord tumor. However, as has been pointed out by others, spinal fluid examination should be done with caution in cases of suspected spinal cord tumors, since there is danger of herniation of the tumor with compression of the cord and increased neurologic deficit. The high incidence of complete removal of the tumors in this series illustrates the need for early diagnosis and treatment before the advent of serious, irreversible neurologic damage. The development of neurologic deficits is well illustrated by the five patients in whom operation was delayed.

SUMMARY AND CONCLUSIONS

1. The diagnosis and localization of intraspinal cord tumors can sometimes be made before definite neurologic changes develop, and it is important to recognize these lesions before serious, irreparable damage to the spinal cord occurs.

2. In a review of 150 verified spinal cord tumors, 37 are reported in this study. Of these, 32 exhibited no definite or localizing neurologic signs at the time operation was performed, and the remaining five were neuro-

logically negative at the time of their original examination but developed definite signs while under observation.

3. The only constant symptom in these patients was that of pain, which was the primary complaint in all cases.

4. The pains were not typical either in character or in location; the duration of illness varied from two months to twenty-seven years; and the ages of the patients ranged from 11 to 72 years.

5. In the vast majority of cases the pain occurred at night or was increased by lying down and could be induced or intensified by coughing, sneezing or straining.

6. Roentgenologic examination of the spinal column indicated the presence of the tumor in ten of the 37 cases.

7. The spinal fluid protein was elevated in 26 of the 29 instances in which it was studied.

8. Myelography was of aid in localization of the spinal cord tumor in 90 per cent of the patients.

REFERENCES

1. Gowers, W. R., and Horsley, Victor: A case of tumour of the spinal cord: Removal; Recovery, Med.-Chir. Tr., Lond. 71:377, 1888.
2. Quincke, H.: Die Lumbalpunction des Hydrocephalus, Berl. klin. Wchnschr. 28:929 and 965, 1891.
3. Froin, G.: Inflammations meningées avec reactions chromatique fibrineuse et cytologique du liquid cephalorachidien, Gaz. d. hôp. 76:1005, 1903.
4. Queckenstedt, E.: Zur Diagnose der Rückermarkskompression, Deutsche Ztschr. f. Nervenh. 55:325, 1916.
5. Ayer, J. B.: Spinal subarachnoid block as determined by combined cistern and lumbar puncture; with special reference to the early diagnosis of cord tumor, Arch. Neurol. & Psychiat. 7:38, 1922.
6. Dandy, W. E.: Ventriculography following the injection of air into the cerebral ventricles, Ann. Surg. 68:5, 1918.
7. Sicard and Forestier: Méthode générale d'exploration radiologique par l'huile iodée (lipiodol), Bull. et mém. Soc. méd. d. hôp. de Paris 46:463, 1922.
8. Steinhausen, T. B.; Dungan, C. E.; Furst, J. B.; Plati, J. T.; Smith, S. W.; Darling, A. P.; Wolcott, E. C., Jr.; Warren, S. L., and Strain, W. H.: Iodinated organic compounds as contrast media for radiographic diagnoses; III. Experimental and clinical myelography with ethyl iodophenylundecylate (Pantopaque), Radiology 43:230, 1944.

● Under the name of athetosis (Αθετος, without fixed position), I propose to describe an affection which, so far as I know, has not heretofore attracted the attention of medical writers, and of which two cases have come to my knowledge. It is mainly characterized by an inability to retain the fingers and toes in any position in which they may be placed, and by their continual motion. From these phenomena, I have applied the term athetosis to the disease, having as yet had no opportunity of ascertaining by post-mortem examination the nature of the lesion to which the symptoms are due.

—William A. Hammond in *A Treatise of Diseases of the Nervous System*, published in 1871.

Role of Birth Injury and Asphyxia in Idiopathic Epilepsy

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It has been suspected for many years that idiopathic epilepsy, or recurrent seizures without apparent cause, may be due to birth trauma. If sufficient attention had been accorded the paper by Little[1] in 1862 much time might have been saved in evaluation of the causal relationship of dystocia to epilepsy. The paper was titled, "On the influence of abnormal parturition, difficult labours, premature birth and asphyxia neonatorum on the mental and physical condition of the child." When Sigmund Freud[2] took up the subject in 1897 he found that almost nothing could be added to Little's contributions. Yet in spite of this work, Little's disease was later described as due to a congenital or developmental defect.

The present writers became acutely interested in the problem of asphyxia and its sequelae in 1933 when studying the case of a boy who had been throttled by a drunken sailor and six months later developed generalized athetosis. Courville then published a monograph on asphyxia secondary to faulty anesthesia,[3] and later studied with Marsh[4] the pathologic findings in brains years after asphyxia. It was shown that convulsions, prolonged coma and choreoathetosis were not the result of the anesthetic but of asphyxia. Studies on microgyria and ulegyria revealed that these conditions were the end result of cortical and subcortical necrosis following asphyxia. Nielsen has studied six clinical cases of asphyxia secondary to circulatory collapse during spinal anesthesia with resultant convulsions, athetosis, hypophrenia and dementia.

Cortical findings are quite different in individual cases, the distinctions being due to processes of repair. Death in a few hours leaves essentially a normal cortex. Death after a few weeks produces a cortex with innumerable very small or even microscopic foci of necrosis. Many months of life after asphyxia allow time for repair with focal cortical scars and cysts. If many years elapse before death, microgyria appear.

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The chain of evidence is not absolutely complete but little doubt of these events remains. Penfield[5] has come to believe that microgyria are the focal points of convulsive seizures in some cases.

EVIDENCE

Aside from coma, the most common single symptom of acute asphyxial states is the array of hyperkinetic phenomena, especially grand mal seizures. The train of symptoms is the same regardless of the mechanism by which central anoxia occurs. Therefore, the acute alterations resulting from lack of oxygen are capable of producing convulsive seizures. Occurrence of cerebral anoxia without seizures may depend on varying degrees of susceptibility to convulsions in different persons. In asphyxiated infants convulsions usually develop within the first few months of life. In such cases which come to autopsy later, unilateral or bilateral atrophies are typically found. It is particularly in such cases that Courville and Marsh[4] found ulegyria.

In cases of ulegyria shown at autopsy there may be no other lesion or there may be microscopic scars. A case recently studied showed acellular cortical areas. On the other hand, changes described by Penfield and Erickson[6] may be present with additional cellular areas identical with those known to be anoxic in origin.

In the past it has been thought that the acellular areas found in the cortex of patients with idopathic epilepsy were the result and not the cause of seizures. They were then ascribed to focal arterial spasm or some other mechanism causing ischemia. This assumption is unproved.

The final proof of the etiologic importance of these acellular areas depends on proof of their presence after neonatal asphyxia and the demonstration of such areas in individuals with generalized electroencephalographic dysrhythmia.

CLINICAL STUDIES

Proof of birth asphyxia is extremely difficult to establish by history. It is common knowledge that many children have minor asphyxial disturbances at birth, but they are relieved by manipulations such as slapping, cleansing of the throat or other simple measures, without any sequelae. Obstetricians know also that greater difficulties often occur, but are resolved after four to seven minutes without any written record of the matter. If the child is made to breathe well in a few minutes it is assumed that the difficulty is past. Thus there is neither written record nor memory in the minds of anyone concerning the very items one needs in a study of asphyxia. In an excellent review Russ and Strong[7] stated

that asphyxia of more than two minutes' duration after birth would leave residuals.

Because of difficulties which seem insurmountable in obtaining a reliable history of asphyxia, Nielsen[8] reasoned that a history of birth sequence would be valuable in showing the effects of dystocia. Since we already know that the firstborn sibling has far more difficulty than those of subsequent birth by the same mother, and since birth primacy can virtually always be established, an opportunity was presented to determine whether idiopathic epilepsy was essentially a problem of birth asphyxia. Accordingly a series was studied and a preliminary report was made of 105 cases. It was found that nearly 60 per cent of epileptics were firstborn. However, the number of siblings in each family was not established and indeed could not be fixed since children were still being born. Since that time another series of 81 cases with 273 siblings has been studied. In that series the number of siblings was arbitrarily taken from those who were not firstborn and the place of the patient in the sibling series was taken as the number of siblings in the family. All error thus would be in favor of fewer rather than more siblings. Even so, there were 3.3 siblings per family. The total number of cases of epilepsy from private practice in this study is now 188, of which the birth sequence is known in 176. The 12 unknown are omitted.

In order to check the same question on a totally different group Nielsen obtained the collaboration of Dr. Fred O. Butler,[9] Superintendent of Sonoma State Home at Eldridge, California, who was able to furnish excellent records of 780 cases in which all factors were known. That series is fraught with hypophrenia, alcoholism in parents, illegitimacy and severe poverty in general. There were 780 epileptics among 3,275 siblings, or 4.2 children per family. Combining these two series of cases there were a total of 374 firstborn out of 956 epileptics, or 39.12 per cent firstborn.

The average number of siblings per family in cases where the fact was determined was 4.1. This figure also is not an absolute one because more children may subsequently be born, but any error would tend to raise and not lower the incidence of birth trauma. Now since 39.12 per cent of cases of epilepsy are in the firstborn, the remaining 60.88 per cent must be divided among the 3.1 remaining siblings. This means 60.88 divided by 3.1, or 19.64 per cent. Firstborn then have a susceptibility ratio of 39.12 to 19.64, or almost exactly 2 to 1. This may be interpreted that in this series the mere fact of being firstborn gave the child twice the susceptibility to epilepsy of any child subsequently born to the same mother.

It is of interest to guess or to attempt to calculate the percentage of firstborn who develop epilepsy. It would seem that about 40 per cent

of all cases of idiopathic epilepsy are in firstborn individuals. Since there are 500,000 epileptics in this country of 140 million inhabitants with about 35 million firstborn, we can assume that 40 per cent of 500,000 or 200,000 of the 35 million firstborn develop epilepsy, or 1 in 175. This means about 0.6 per cent of firstborn have epilepsy. An equal number, roughly estimated, are spastic. Thus 1.2 per cent of firstborn suffer from either epilepsy or spacticity with or without choreoathetosis. Of course, children subsequently born may also have asphyxia or birth trauma but much less danger exists.

The first question to arise is, if firstborn are twice as susceptible to epilepsy as those of subsequent birth, why does cerebral dysrhythmia run in families? It is granted that the cerebral dysrhythmia indicates a predisposition to epilepsy but of itself it is not epilepsy. Probably in such families birth trauma, especially asphyxia, becomes the factor which provokes seizures. Since less than one per cent of firstborn become epileptics, it is clear that birth trauma alone is rarely an adequate cause. It can, however, be an adequate cause in a predisposed individual.

The question of lapse of time between birth asphyxia or injury and the onset of convulsions is important. If the cases are divided into quinquenniums it is found that the greatest incidence is in the first five years, slightly less in the second, definitely less in the third and much less in the fourth five-year period. Convulsions beginning after the age of 20 are rarely due to trauma at birth. There are still problems calling for extended research in this field.

In cases of gross cerebral trauma at birth, no one will question that surgical intervention as soon as possible is indicated. In cases of asphyxia years may elapse before it is recognized as having occurred. The question of surgery then depends on the site and extent of cerebral damage. In the infant asphyxial lesions of the basal ganglia usually produce choreathetosis, while cortical lesions produce epilepsy. An idiopathic epileptic is then probably susceptible of exploration to determine the exact epileptogenic focus. The best clinical guide to the site is the aura. If only one gyrus were affected the problem would be relatively simple, but there are often several foci. Excision of the focus depends largely on its site. In the frontal or temporal region excision is theoretically not difficult if the focus is determined. In children under the age of 10 speech areas can be resected with impunity; the older the patient after that age the greater the hazard. Aphasia, from which the young patient can recover, is a small matter compared to epilepsy. However, in the occipital region or in the motor cortex it may be better to avoid excision rather than produce a large visual defect or focal paralysis. Impossible or inadvisable

areas for surgical intervention are relatively few. It would seem, therefore, that every idiopathic epileptic is potentially a surgical case.

SUMMARY AND CONCLUSIONS

1. There is strong evidence from both the clinical and pathologic viewpoints that idiopathic epilepsy is due to small cortical focal areas of damage in individuals with lowered convulsive thresholds.

2. Firstborn children, because of difficulties during birth, are twice as susceptible to epilepsy as are children subsequently born to the same mother.

3. Children of subsequent birth may suffer from exactly the same difficulties at birth as do the firstborn, and consequently they may also have epilepsy due to birth trauma or asphyxia.

4. The focal lesion resulting from asphyxia or birth trauma acts as a trigger mechanism, but is not adequate to produce epilepsy in all persons. A lowered convulsive threshold, as indicated by cerebral dysrhythmia, is necessary in many instances.

5. Estimates indicate that 40 per cent of all cases of idiopathic epilepsy are in firstborn children. A smaller percentage of those subsequently born also develop epilepsy because of birth trauma. Probably more than one-half of all cases of essential epilepsy are the result of birth injury or asphyxia. The remainder are due to a variety of causes of cerebral damage.

6. In the conviction that there is a cerebral focal lesion mechanism in each case of idiopathic epilepsy, the authors believe that each case should be evaluated from the standpoint of surgical intervention. Even though surgical intervention may be successful only in a minority of cases, it should be considered.

REFERENCES

1. Little, W. J.: On the influence of abnormal parturition, difficult labours, premature birth and asphyxia neonatorum on the mental and physical condition of the child, Tr. Obstet. Soc. London, 3:293, 1862.
2. Freud, S.: Die infantile Cerebrallähmung, Nothnagels Handbuch, Berlin, Holder, 1897.
3. Courville, C. B.: Asphyxia as a consequence of nitrous oxide anesthesia, Medicine, 15:129, 1936.
4. Courville, C. B., and Marsh, C.: Neonatal asphyxia; Its encephalic residuals and mechanism of their production, Bull. Los Angeles Neurol. Soc. 9:121, 1944.
5. Penfield, W., and Humphreys, S.: Epileptogenic lesions of the brain, Arch. Neurol. & Psychiat. 43:240, 1940.
6. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Illinois, Charles C. Thomas, Publisher, 1941.
7. Russ, J. D., and Strong, R. A.: Asphyxia of newborn infants, Am. J. Ob. and Gyn., 51: 64, 1946.
8. Nielsen, J. M.: Etiology of idiopathic epilepsy, Bull. Los Angeles Neurol. Soc. 11:97, 1946.
9. Nielsen, J. M., and Butler, F. O.: Birth primacy and idiopathic epilepsy, Tr. Am. Neurol. A. 72:201, 1947; Bull. Los Angeles Neurol. Soc. 13:176, 1948.

Polycythemia Vera and the Nervous System

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POLYCYTHEMIA vera is not a common disease, yet its clinical and pathologic features are such that it should be considered in the differential diagnosis of many neuropsychiatric syndromes. Our purpose is to emphasize those aspects of polycythemia which indicate nervous system involvement or which produce functional symptoms that may be mistaken for psychiatric disease.

The etiology of polycythemia vera is unknown. Its basic pathologic defect is overproduction of blood cells in the bone marrow. There is marked vascular engorgement throughout the body, and hemorrhages and thrombosis with infarction may occur anywhere. Symptoms are due to circulatory stasis with tissue anoxia and to disturbances of function secondary to the vascular lesions.

Chief clinical characteristics of the disease are an increase in red blood cells, dusky red cyanosis of the skin and an enlarged spleen. The onset is insidious, and first symptoms of headache, dizziness, tinnitus or visual disturbances are usually noted in middle or later life. Some patients complain first of dyspnea, weakness or anorexia; vague gastrointestinal disturbances, peptic ulcers and gastric hemorrhages are common. Many other symptoms involving all organs and organ systems of the body are noted. The face is almost always flushed, ecchymoses of the skin are frequent, the blood is dark and thick, red cell count is usually above 6,000,000 per cu. mm., and hemoglobin is well over 100 per cent (16 grams). A markedly elevated hemotocrit is a characteristic finding. The white blood cell and platelet counts and blood volume are all increased, and the basal metabolic rate is often elevated.

The course of the disease is chronic, and patients may suffer from repeated vascular lesions before a vital organ is involved. A vascular accident, anemia secondary to fibrosis of the bone marrow, or occasionally

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transformation of polycythemia into leukemia are the chief causes of death.

NERVOUS SYSTEM PATHOLOGY

The principal nervous system lesions in polycythemia result from marked generalized vascular congestion. Cerebrovascular accidents are common and are a frequent cause of death. Cabot in 1899[1] reported the first case of cerebral apoplexy attributed to polycythemia, showing at autopsy a large extradural hemorrhage originating from rupture of the middle meningeal artery. Other cases of intracerebral hemorrhage have been cited[2, 3, 4] and subdural and subarachnoid hemorrhages have been seen occasionally.[5, 6, 7, 8] By far the most common lesions are those secondary to thrombosis, very often multiple. Hutchinson and Miller in 1906[9] reported the first complete pathologic study of the brain in polycythemia. Their case showed extensive thrombotic softening in both occipital lobes, the tip of the left temporal lobe, the left lenticular nucleus and the right thalamus. Jacobs[10] recorded a case with hemiplegia which at autopsy had a large softening in the left frontal lobe, a smaller one in the right lenticular nucleus, and a hemorrhagic pachymeningitis. Ford[11] described a case with thrombosis of the right middle cerebral artery and superior longitudinal sinus, exhibiting also a small infarct in the left motor cortex from a previous thrombosis. Winkelman and Burns[12] described a case in which there was enormous distention of the capillaries and small vessels, with perivascular hemorrhages, edema and diffuse degenerative changes of the ganglion cells.

In other cases the vessels are not markedly distended, and the principal changes are those of tissue infarction with necrosis and acute and chronic encephalomalacia. While microinfarcts are seen frequently, the lesions usually described result from thrombosis of the medium sized and larger vessels. Proliferative and inflammatory vascular changes are minimal.

A marked tendency to thrombosis is due presumably to the huge increase in blood cells and blood volume. Viscosity of the blood is greatly increased and the rate of flow is lessened correspondingly.[13, 14] Increase in platelets and in serum calcium which occurs in polycythemia may further predispose to intravascular clotting.[15] Arteriosclerosis has also been regarded as a factor which intensifies the likelihood of thrombosis. Polycythemia occurs in that age group in which vascular pathology is usually present, and there is some evidence that the polycythemia hastens the progression of arteriosclerotic disease.[16]

In many cases having obvious focal areas of necrosis, a careful search does not reveal any vascular pathology.[17, 18] It is postulated that the pathologic lesions result from tissue anoxia secondary to sluggish circulation. It is well known clinically that focal disturbances may recur repeatedly before a permanent disability results. These disturbances are assumed to be due to a temporary focal anoxia. It is also possible that they are secondary to small and unrecognized thrombi, accompanying which there is a more widespread but temporary interruption of function.

NERVOUS SYSTEM SYMPTOMATOLOGY

The importance of nervous system symptomatology in polycythemia was stressed by Vaquez in 1892 in the first published case of the disease.[19] His patient developed in the course of the illness severe Ménière-like crises marked by vertigo, tinnitus of the right ear, a staggering gait and vomiting. Osler in 1903[20] noted marked nervous system symptoms in eight of nine cases. Headache was a prominent symptom in four, pains in the back and abdomen in three cases. Other symptoms included vertigo, tinnitus, a feeling of fullness in the head, pains and paresthesias in the extremities, speech disturbances, gait difficulties, weakness, blurred vision and loss of consciousness.

Many reports of polycythemia followed these earlier studies, and it became obvious that involvement of the nervous system was a cardinal feature of the disease. In 1912 Lucas[2] summarized 179 known cases in which the most prominent symptoms were florid skin (83 per cent); symptoms of cerebral congestion such as headaches (31 per cent); dyspnea (19 per cent); and lassitude and weakness (19 per cent). Many nervous system complaints and symptoms were noted indicating disturbances in the motor pathways, extrapyramidal system, speech and visual centers, brain stem and meninges. A great variety of psychiatric complaints were recorded as well, including apprehension, delirium, confusion, insomnia, memory loss and psychosis.

Harrop in 1928[4] stated that "the nervous and psychic symptoms of the disease, together with the disturbances of the special senses, are often its first and most striking manifestations." Dameshek and Henstell in 1940[21] emphasized that symptoms referable to the central nervous system were present in almost every case. In a study of 163 cases of polycythemia by Tinney, Hall and Giffin,[22] 127 or 78 per cent of the patients had nervous system symptoms, and in 55 patients (34 per cent) the reason for seeking medical attention was neurologic in nature.

NONLOCALIZING NEUROPSYCHIATRIC SYMPTOMS

In most cases of polycythemia the symptoms which suggest nervous system pathology are vague, multiple and misleading. The most common group of complaints are headache which is noted in almost all patients, vertigo, fatigue and weakness. Headache varies from a sense of fullness within the head to severe attacks of pain identical to migraine. Vertigo may consist merely of a sensation of giddiness or lightheadedness, or it may be accompanied by a sense of turning, by a staggering gait and by nausea and vomiting such as is seen in labyrinthine disease.

Other symptoms frequently noted are visual disturbances, paresthesias and pains in the limbs. Fainting spells and convulsions occur occasionally. Oppenheimer[23] described a case in which polycythemia was considered the cause of a grand mal epileptic disorder.

Many vague symptoms occur which do not indicate any obvious disease. These symptoms are usually multiple and are combined with equally vague gastrointestinal, circulatory, respiratory and genitourinary complaints. They include chronic lassitude and fatigue, anorexia, nausea, abdominal pain, dyspnea, palpitation, hot or cold hands and feet, somnolence, nervousness and irritability, insomnia, frequency and urgency and scattered aches and pains. A patient with these complaints is likely to be labeled a "neurotic," particularly when the usual manifestations of polycythemia are minimal.[24] One patient described by Sloan[6] had previously been given the diagnoses of neurasthenia, psychasthenia, and melancholia, and had been psychoanalyzed for a time without effect on his symptoms before polycythemia became evident. Tinney, et al.[22] found that almost all patients in their series had vague symptoms and that 17 per cent of them had symptoms suggesting severe neuroses and exhaustion. Insomnia or drowsiness were major complaints in 14 cases (8 per cent), and mental depression was present in seven cases.

Psychiatric disturbances, aside from those which might be confused with a neurosis, are most frequently related to disorders in the sensorium. Difficulty in concentration and in memory is a common complaint.[17] In some cases transient lapses in memory have occurred, lasting from a few minutes to several days,[4, 21, 25] while in others memory loss is present continually.[12] Mental deterioration may become severe and the patient may become completely irrational and confused.[26, 27] Levin[28] gathered ten cases in which depression was the outstanding feature. Bizarre olfactory hallucinations may occur occasionally.[29, 30]

The striking feature of these neurotic and psychotic phenomena is that they frequently disappear completely when the blood volume is re-

turned to normal.[4, 6, 18, 21] This emphasizes the fact that many of the symptoms are caused by functional impairment secondary to the generalized congestion, as opposed to structural changes associated with definite vascular lesions.

Case 1.—C. P., a farmer aged 55, was first seen at the outpatient clinic in November 1940, complaining of excessive weakness and fatigue of three months' duration. He also complained of occasional headaches, difficulty in thinking and memory loss. He had no other complaints and previously had been in excellent health. Physical and neurologic examinations were normal. Blood pressure was 132/94; hemoglobin, 98 per cent; red cell count, 4,860,000 per cu. mm.; and hematocrit reading, 47 per cent. A tentative diagnosis of cerebral arteriosclerosis was made and he was advised to limit his activities slightly. In 1941 the patient's wife stated that he was more irritable than normal and exhibited noticeable emotional instability. A plethoric appearance was observed at this time, but the blood was not examined. He was placed on phenobarbital medication. In 1943 the patient noted numbness in the left hand after milking and episodes of vertigo upon arising. He was doing routine farm work at this time, though he had to rest several times during the day. In 1944 his lassitude and weakness had progressed and he began to notice definite lapses of memory. At this time hemoglobin was 20 grams, red count 5,550,000 per cu. mm. and the hematocrit 51 per cent. A complete cardiac examination was negative.

In 1945 the diagnosis of polycythemia was finally considered. It was found that the patient obtained considerable relief from fatigue following withdrawal of a pint of blood. Up to that time his case had been followed in the neuropsychiatric clinic, but he was then transferred to the medical and hematology clinics. From 1945 to the present he has been observed closely and has been hospitalized once. Treatment has consisted of venesection, phenylhydrazine and radioactive phosphorus. Hemoglobin has been kept at 16 or 17 grams, and the hematocrit has been about 50 per cent. All symptoms disappeared with this treatment routine and he has been doing his farm work without rest periods.

Comment: The characteristically vague and insidious onset of polycythemia is well illustrated in this case. The patient was followed in a neuropsychiatric clinic for four years before the exact diagnosis was made. Symptoms of fatigue, irritability, emotional instability, headaches, memory difficulty, numbness and vertigo could easily be confused with a neurosis, particularly if the patient were a complaining type. To be noted also is the fact that the patient had symptoms for several years before blood values became markedly abnormal. It is unnecessary to stress the value of complete initial and occasional follow-up evaluations in patients observed for long periods of time, particularly when their symptoms increase gradually.

FOCAL NEUROLOGIC COMPLICATIONS

Hemiplegias: The most common focal lesions in polycythemia, aside from visual disturbances and vertigo, involve the motor pathways. Various degrees of hemiplegia, with or without aphasia, occur. Hemiplegias are usually the result of vascular thrombosis, and they occur most often after the diagnosis of polycythemia has been established for

some time. All degrees of motor loss may occur, from slight weakness in one limb to complete paralysis of arm and leg.[17, 31, 32, 33, 34] Various visual field defects may also be exhibited.[24] The thalmic syndrome in polycythemia has been described by Alajouanine, et al.[35] Transient or permanent attacks of hemianesthesia are as common as motor disturbances.

Occurrence of bilateral hemiplegia or of several focal motor and sensory lesions is not unusual.[18, 36] Transient paralyses and aphasias are even more common. Howell[37] described a case in which there were five temporary episodes of aphasia before hemiplegia developed. Weber[38] reported a case in which there were eight attacks of temporary aphasia over a year's time, and nine years later the patient suddenly noticed numbness over the whole right side of his body. Occasionally, hemiplegia provides the first indication of the underlying disease. This was true for the patient described below.

Case 2.—E. T., a farmer aged 36, developed a moderately severe headache on August 10, 1948. This continued for several days. On August 15 he noted nausea and vomiting and became lethargic. He was hospitalized the following day when he became unable to talk or use his right arm. Past history revealed that he had had mild but definite memory loss for several months, and on several occasions he had complained of numbness of his hands. Two years previously he had experienced an episode of ankle edema and was told that he had "kidney disease." Examination revealed an expressive and receptive aphasia, weakness of the right arm and lower face, and pathologic reflexes on the right. Physical examination showed enlargement of the spleen. Hemoglobin was 18 grams; red cell count, 6,360,000 per cu. mm.; hematocrit, 56.5 per cent. Other studies were negative. The clinical diagnosis was polycythemia complicated by thrombosis of a branch of the left middle cerebral artery. Treatment by venesection was instituted, but it was difficult to maintain normal blood levels.

A few days after admission the patient became more alert and began to understand simple statements. He gradually improved and was beginning to talk when, eight days after admission, aphasia again became complete and hemiplegia extended to the right leg. No pulsation of the left carotid artery could be detected, and it was assumed that a thrombus had occluded the common carotid artery.

The patient again began to improve but two weeks later developed a pulmonary infarct. Three months later he expired following a thrombosis of the superior mesenteric artery. Autopsy revealed an infarction of the entire small bowel. A recent myocardial infarct was present. Vascular thromboses were scattered throughout the viscera. The left common carotid artery was completely occluded by a thrombus extending from near its origin to the bifurcation. Examination of the brain revealed multiple areas of softening in the distribution of the left middle cerebral artery. There was also a small area of encephalomalacia in the right middle frontal gyrus. Microscopically, these areas were typical ischemic infarcts. There were no inflammatory or endarteritic changes.

Comment: In this patient diagnosis of polycythemia was not made until a cerebral thrombosis had occurred. Prior to this, symptomatology was vague consisting of memory loss and numbness of the hands. The transient nature of the first stroke followed by a more permanent and extensive lesion is characteristic in polycythemia.

Post-mortem examination demonstrated bilateral lesions in the brain. The one in the right frontal lobe was in a relatively silent area, but may have been responsible for his complaint of difficulty with memory. Thrombosis of the carotid artery in polycythemia is not common but does occur. Low and Poppen[39] in 1908 described a case with almost identical clinical and pathologic findings.

Basal Ganglia Lesions: Symptoms indicating involvement of the basal nuclei are seen occasionally. Several reports describe the development of choreiform movements during the course of the disease.[40, 41] In one of these[42] the chorea disappeared dramatically following irradiation to the long bones. Doll and Rothschild[43] reported the case of a 44 year old male who had polycythemia and a syndrome resembling Huntington's chorea. A case complicated by chorea, cataplexy and mental confusion has been cited by Schiff and Simon.[44] A clinical picture resembling Wilson's hepatolenticular degeneration was seen in one patient described by Brockbank,[24] and a parkinsonian tremor was present in another examined by Damashek and Henstell.[21]

Diencephalic Lesions: Hypothalmic and pituitary disturbances occur occasionally in patients with well established diagnoses of polycythemia. The reverse situation in which polycythemia appears to result from diencephalic lesions has also been described, and considerable discussion has developed concerning the possibility of an erythrocyte stimulating center in this area.

Several case reports of narcolepsy and obesity as complications of polycythemia have been recorded.[45, 46, 47] Gunther[48] described a case of polycythemia with obesity, narcolepsy and diabetes insipidus, and Lhermitte and Peyre[49] recorded a case with narcolepsy, cataplexy and attacks of chills and generalized tremors. Keschner[50] described a case in which the patient experienced exaggerated salivation, flushes of heat and cold, and marked hyperhidrosis over the upper half of the body.

Cases of polycythemia associated with or secondary to other diencephalic disturbances are somewhat more common and have been noted following encephalitis lethargica[51, 52] and brain trauma.[53, 54] A number of cases occurring with pituitary and hypothalamic lesions have also been observed.[55, 56, 57, 58] Guillain, et al.[54] found mild polycythemia associated with the adiposogenital syndrome, diabetes mellitus, diabetes insipidus, narcolepsy and acromegaly. Moehlig and Bates[59] described two cases of polycythemia and pituitary basophilism, one having a basophilic adenoma while the other had a suprarenal tumor. Cushing[60] had previously noted a tendency to polycythemia in cases of pituitary basophilism. Barker and Craig[61] reported two cases in which polycythemia was associated with tumors in the region of the third ventricle. They felt that

polycythemia was produced by a disturbance in water metabolism, concentrating the blood with a low plasma volume. Further evidence for a possible erythrocyte stimulating center has been produced by Schulhof and Matthies,[52] who were able to cause polycythemia in rabbits by introducing foreign material into the diencephalic region.

Polycythemia has also been described in association with lesions in other areas of the brain. Drew and Grant[5] gathered ten such cases, including sarcoma of the convexity of the left frontal lobe (Salus[62]), glioblastoma multiforme of the right parietal lobe (Meiner[63]), and "endothelioma" of the right frontal region (Galindez and Sanguinetti[64]). In their own case a large chronic subdural hematoma was present, and they were unable to ascertain whether the original disease was polycythemia or whether the increase in blood cells was secondary to the hematoma. In four cases the lesions were in the posterior fossa. Oppenheimer[23] mentioned a case in which a cerebellar medulloblastoma was found at autopsy. Carpenter, Schwartz and Walker[65] described three cases in which the polycythemia disappeared after removal of cerebellar hemangioblastomas.

The common factor in all these cases of tumor in areas of the brain other than the diencephalic region was a marked increase in cerebrospinal fluid pressure. It is quite possible that this increased pressure might have been transmitted from the third ventricle to neighboring hypothalamic centers which influence water balance or erythropoietic activity. On the basis of the above evidence, a number of authors suggest that there is a center for stimulation of erythrocytes located in the diencephalon.[55, 62, 65, 66] Lucia and Marasse,[67] on the other hand, conclude that the relationship of polycythemia to diencephalic lesions is more fortuitous than real. It is obvious that further study of this problem is necessary.

Polycythemia Confused with Brain Tumor: In some cases cerebral complications of polycythemia closely resemble symptoms of brain tumor. When lesions are focal and slowly progressive, and when there is a papilledema and increased spinal fluid pressure, the diagnosis between polycythemia and tumor is exceedingly difficult.[21] One of the cases described by Christian[18] was explored for a possible tumor despite knowledge that the patient had polycythemia. Naville and Bru⁺sch[68] described a case in which a 33 year old woman developed hemiplegia with aphasia secondary to polycythemia. Ten years later she developed convulsive seizures, headaches and papilledema. Though a diagnosis of tumor was made, none was found. Oppenheimer[23] reported a case in which findings led to an operation for brain tumor. An area of softening was found. A year later the patient developed the typical picture of polycythemia vera. Adams[69]

examined a patient in whom focal seizures were present. There was a history of a slight head injury and the patient was subsequently explored, but with negative results. Brockbank[24] and Drew and Grant[5] have also described cases in which surgical exploration was undertaken because there was a question that the symptoms were caused by a tumor. Tinney, et al.[22] found that in eight of 127 cases a brain tumor was suspected, and that in two cases a tumor was found.

It is generally agreed that, in a case of polycythemia with symptoms suggestive of tumor, the blood volume and cell count should be restored to normal before exploration is undertaken. In most cases symptoms will disappear under such therapy. It must be kept in mind, however, that a tumor or subdural hematoma may occasionally be present, even in obvious cases of polycythemia vera.

Visual Disturbances: Complaints referable to the visual system are among the most common of all symptoms in polycythemia. A gradual and progressive blurring or dimness of vision may be the initial symptom of the disease. Transient periods of loss of vision or even complete blindness may occur.[18, 69, 70] Loman and Dameshek[71] repeated the description of a case reported in 1838 of amaurosis from plethora in which the patient suffered from momentary attacks of visual loss, eventually terminating in blindness. Partial vision was restored by bloodletting. Many patients notice lights and spots before the eyes, and when these occur with headache the diagnosis of migraine is apt to be made. Diplopia is another common complaint. Stewart[72] cited a case in which there was hemiplegia, aphasia and blindness from bilateral "optic neuritis." Douglas and Eisenbrey[73] described a case in which there were transient attacks of complete blindness in one eye, with the ophthalmoscopic examination negative. Brockbank[24] recorded a case in which visual failure with bilateral optic atrophy followed a head injury, but an exploration was negative.

Funduscopic examination reveals engorgement and cyanosis of the retinal veins.[38, 74, 75] Hemorrhages are seen occasionally,[75] and thrombosis of the central retinal vein may occur.[76] Blurring of the disc margins is often present, and definite papilledema is not uncommon[2, 41, 77] Drew and Grant[5] collected from the literature 19 cases of polycythemia with papilledema. The diagnosis of brain tumor may be suggested, particularly if focal neurologic symptoms are present as well.[78] Tinney, et al.[22] found engorgement of the veins in almost all of the cases they studied and choked discs were found in eight of the 163 cases.

Case 3.—E. V., a man aged 57, experienced several transient attacks of sudden blindness in the left eye in January 1936. In February 1936 the blindness lasted one month, followed by a slight return of central vision. About the same time he noted

difficulties in concentration and memory and weakness and numbness in the right arm. In February 1937 he began to notice periods of blurred vision in the right eye. Physical examination in April 1937 was negative except for a slightly enlarged liver; blood pressure was 114/80. Examination of the right optic fundus revealed a congested nerve head with dilated veins. An old hemorrhage was seen in the temporal half of the retina. Primary optic atrophy was present in the left eye. The only vision remaining on the left was limited to a small paracentral area. Hyperreflexia and slight weakness of the right arm was noted, and there was obvious memory loss and difficulty in concentration. Laboratory studies revealed hemoglobin, 146 per cent; red blood cell count ranging from 6,200,000 to 8,900,000 per cu. mm.; hematocrit, 76 per cent; and blood volume, 7 liters. Spinal fluid studies were negative. An electrocardiogram revealed evidences of an old myocardial infarct, and roentgenograms revealed a duodenal ulcer. The patient was treated with venesection and phenylhydrazine, and restoration of normal blood levels resulted in considerable subjective improvement. In a follow-up letter two years later, it was reported that the patient had become almost completely blind.

Brain Stem Lesions: Vascular lesions localized to the region of the brain stem may also be expected. The most common symptom is vertigo, which is probably caused in many cases by distention of the vessels of the labyrinth. Vertigo is a major complaint in at least a third of all cases.[2, 22] It was present in fourteen of the twenty cases described by Dameshek and Henstell.[21] It is often associated with tinnitus and hearing loss, and sometimes with nausea and vomiting and other symptoms common to Ménière's syndrome. Occasionally the complaint of vertigo is the initial symptom, and it may be the only complaint for some time (Christian,[18] Cole[79]). Progressive deafness, often unilateral[1], is not infrequent in polycythemia (Dameshek and Henstell[21] and Adams[69]). Tinnitus is very common. Diplopia and nystagmus are less frequent. Cerebellar disturbances may also occur.

Case 4.—R. S., aged 42, first noted tinnitus and gradual hearing loss in the right ear in 1942. In 1943 he observed bilateral varicosities in his legs, and the left leg tired easily. In 1945 he began to complain of a progressive feeling of fatigue and ill health, accompanied by occasional fainting spells after exertion. In the summer of 1949 he became increasingly irritable. In September he had several transient attacks of diplopia, and in October he began to have difficulty in coordinating the fingers of his left hand. He also noted numbness of the left arm and leg. Examination upon admission in November 1949 revealed a slightly obese man with a florid face. There were marked varicosities in the legs and left arm. The spleen was easily palpable. Neurologic findings included engorged retinal veins, bilateral horizontal nystagmus, nerve deafness of the right ear and slowness of movement of the tongue. There was moderately severe cerebellar involvement of the left arm and leg, including cerebellar rebound and left sided hyporeflexia. Deep sensation was poor in the left leg.

Laboratory studies showed hemoglobin, 22.8 grams; hematocrit, 71 per cent; increased leukocyte and platelet count. Spinal fluid was normal with a normal pressure. An electroencephalogram, visual fields, skull roentgenograms and vestibular tests were normal. Audiometric tests revealed marked nerve deafness on the right.

Withdrawal of 500 cc. of blood was accompanied by a marked increase in the patient's sense of well being. Neurologic signs were only slightly improved.

Comment: In this patient there were obviously several lesions, including one involving the left cerebellar hemispheres and one involving the right eighth nerve. His follow-up has been too brief to show whether there will be any great improvement in his neurologic symptoms under continued treatment.

Spinal Cord and Peripheral Nerve Lesions: Isolated involvement of the spinal cord in polycythemia has not been reported, though there is no reason why thrombosis of the spinal arteries with resulting disturbance of function should not occur. Spinal fluid examinations are negative except for occasional cases in which there is increase in spinal fluid pressure. Bottner[80] recorded several cases with increased pressure, one having a value as high as 540 mm. of water. Drew and Grant[5] described a patient in whom the spinal fluid pressure was 510 mm. of water. Lohman and Dameshek[71] recorded a pressure of 380 mm. of water, with a return to normal following removal of 3,000 cc. of blood. The increased pressure presumably results from the fact that the bony skull case prevents brain tissue from expanding when vessels are engorged. Decompression, however, was of little benefit to the patient described by Drew and Grant.

Symptoms of peripheral nerve involvement in polycythemia are striking, but actual cases of mononeuritis or multiple neuritis are rare. A definite case of brachial plexus neuritis was described by Meyer,[81] and Fetterman and Spitteler[82] published a case in which mononeuritis in the leg was associated with polycythemia. Pains in the limbs are common and in some cases they are severe. They seldom resemble root pains, and it has been suggested that they result from local tissue engorgement.[83] In many cases the pains are due to claudication secondary to peripheral arterial disease.[14] Hot or cold sensations in the limbs are common. In some patients the pains are localized to the joints, suggesting arthritis.[21]

Numbness and tingling of the hands and feet are frequent complaints. Dameshek and Henstell[21] found such paresthesias in twelve of twenty patients. In four of nine patients examined by Adams[69] paresthesias were prominent symptoms. These symptoms almost always disappear under treatment. Sturgis,[84] for example, had a patient who always knew when to return for additional venesection by reappearance of numbness in the hands and feet.

Actual atrophy from peripheral neuritis is rare. However, Crosetti[85] reported a case of progressive atrophy of the hands and feet due to peripheral nerve involvment. The patient also had chorea. Christian[18] found a toe drop in one of his patients, and Lhermitte[17] included peripheral atrophy as an infrequent complication in his case studies.

Case 5.—F. H., a woman aged 36, was hospitalized in February 1948 with complaints of progressive weakness in the legs for nine months, weakness of the right arm for six months, hyperesthesias in the hands and feet for two months and inability to walk for the past three weeks. Examination upon admission revealed a patient with dusky cyanosis of the skin and an enlarged liver and spleen. Bilateral papilledema was present. Severe generalized peripheral neuritis was noted. Reflexes were absent and there was marked weakness in all limbs, most severe distally. A glove and stocking loss of all sensation was in evidence. Hemoglobin was 18.5 grams; red blood count, 6,190,000 per cu. mm.; and hematocrit, 60 per cent. Spinal fluid pressure was 16 mm. of mercury and spinal fluid protein was 86 mg. per cent. Basal metabolic rate was plus 45. Sternal marrow biopsy was compatible with the diagnosis of polycythemia.

The patient was treated with repeated venesections and blood values returned to normal. Peripheral neuritis was not changed, however, though she also received intensive physiotherapy and vitamin therapy. She frequently complained of headaches and marked lassitude. In June 1948 she developed abdominal pain with vomiting. She suddenly expired after aspirating some vomitus. Autopsy was refused.

Comment: In this case the chief symptomatology was that of severe peripheral neuritis. This was not influenced favorably by a return of blood values to normal, nor by the usual vitamin and physical treatments. A similar case was studied in the hospital three years previously. Restoration of normal blood values also had no effect on neuritis.[86] The cause of this neuritic picture was assumed to be due to inadequate nutrition or oxygenation of the smaller nerves secondary to generalized vascular congestion which was present.

SUMMARY

Nervous system involvement in polycythemia is a cardinal feature of the disease. Nervous system symptoms are present in at least three-fourths of all cases. In a third of all cases, neurologic symptoms are the most important complaint. The most common symptoms are nonspecific and include headache, vertigo, fatigue and weakness. Visual disturbances, paresthesias and vague aches and pains are frequent. These symptoms are often combined with many other complaints, and a diagnosis of neurosis is easily and often made. A confusional type of psychosis may develop occasionally. Many of these symptoms disappear when the blood values are restored to normal.

Objective neurologic findings are present in over one-fourth of patients with nervous system symptoms. They are usually focal in nature, caused by vascular thrombosis. Hemiplegias are most common, but extrapyramidal syndromes may also occur. Two important characteristics of the cerebral lesions are, first, their occurrence in multiple areas of the brain, and second, the occurrence of repeated thromboses followed by more or less complete recovery. In some cases lesions appear to be progressive. These may be mistaken for brain tumor, especially if increased spinal fluid pressure with choked disc is present.

Occasionally diencephalic lesions are associated with polycythemia. An erythrocyte stimulating center in this area of the brain is postulated, but further investigation of this problem is required before any conclusions can be drawn.

Paresthesias are common complaints but actual peripheral neuritis is rare. A case with a generalized peripheral neuritis and polycythemia is presented.

A series of five personal observations, one with autopsy, are cited to illustrate various neurologic complications of polycythemia.

REFERENCES

1. Cabot, R.: A case of chronic cyanosis without discoverable cause, ending in cerebral hemorrhage, Boston M. & Surg. J. 141:574, 1899.
2. Lucas, W.: Erythremia or polycythemia with chronic cyanosis and splenomegaly, Arch. Int. Med. 10:597, 1912.
3. Zadek, I.: Erythromegalie bei Polycythaemia vera, Berl. klin. Wchnschr. 55:1193, 1918.
4. Harrop, G. A.: Polycythemia, Medicine 7:291, 1928.
5. Drew, J., and Grant, F.: Polycythemia as a neurosurgical problem: A review with reports of two cases. Arch. Neurol. & Psychiat. 54:25, 1945.
6. Sloan, L.: Polycythemia rubra vera: Neurologic complications, Report of four cases, Arch. Neurol. & Psychiat. 30:154, 1933.
7. Tizianello, G.: Spontaneous hemorrhage of the leptomeninges and polyglobulia, Gior. di med. 2:855, 1930, quoted by Sloan.[6]
8. Strauss, I., and Tarachow, S.: Prognostic factors in spontaneous subarachnoid hemorrhage, Arch. Neurol. & Psychiat. 38:239, 1937.
9. Hutchinson, R., and Miller, C.: A case of splenomegalic polycythemia, with report of post-mortem examination, Lancet, 1:744, 1906.
10. Jacobs, C.: Zwei weitere Beitrage zur primaren Polycythamie und deren Genese, München. med. Wchnschr. 59:2384, 1912.
11. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Illinois, Charles C. Thomas, 1945.
12. Winkelman, N. W., and Burns, M. A.: Polycythemia vera and its neuropsychiatric features, J. Nerv. & Ment. Dis. 78:587, 1933.
13. Dameshek, W.: Physiopathology and course of polycythemia vera as related to therapy, J. A. M. A. 142:790, 1950.
14. Brown, G., and Giffin, H.: Peripheral arterial disease in polycythemia vera. Arch. Ind. Med. 46:705, 1930.
15. Brown, G., and Roth, G.: The reduction of hypercalcemia in cases of polycythemia vera by phenylhydrazine. J. Clin. Investigation 6:159, 1928.
16. Norman, I., and Allen, E.: The vascular complications of polycythemia, Am. Heart J. 13:257, 1937.
17. Lhermitte, J.: Les manifestations nerveuses de la polyglobulie. Gaz. d. hôp. 103:661, 1930.
18. Christian, H.: The nervous symptoms of polycythemia vera, Am. J. M. Sc. 154:547, 1917.
19. Vaquez, H.: Sur une forme spéciale de cyanose s'accompagnant d'hyperglobulie excessive et persistante, Compt. rend. Soc. de biol. 44, 384, 1892.
20. Osler, W.: Chronic cyanosis with polycythemia and enlarged spleen: A new clinical entity, Am. J. M. Sc. 126:187, 1903.
21. Dameshek, W., and Henstell, H. H.: The diagnosis of polycythemia, Ann. Int. Med. 13:1360, 1940.
22. Tinney, W. S.; Hall, B. E., and Giffin, H. Z.: Central nervous system manifestations of polycythemia vera, Proc. Staff. Meet., Mayo Clin. 18:300, 1943.
23. Oppenheimer, B.: Vascular occlusion in polycythemia vera, Tr. A. Am. Physicians 44:338, 1929.
24. Brockbank, T.: Neurological aspects of polycythemia vera, Am. J. M. Sc. 178:209, 1929.
25. Freund, H.: Polyzythämie mit ausgang in Perniziose Anämie, München. med. Wchnschr. 66:84, 1919.
26. Weber, F. P., and Watson, J.: Chronic

polycythemia with enlarged spleen, probably a disease of the bone marrow, Tr. Clin. Soc. London. 37:115, 1904.

27. Freund, C.: Polyzythämie, Berl. klin. Wchnschr. 51:1616, 1914.
28. Levin, M.: Erythremia (polycythemia) with a psychosis, Am. J. Psychiat. 10:407, 1930.
29. Muller, E.: Uber Psychische Störungen bei Polyzythämie, Fol. haematol. 9:233, 1910.
30. Steiffler, G.: Uber Dammerzustände von epilepsieartigem charakter bei Polycythemia rubra, Deutsche Ztschr. f.d. ges. gerichtl. Med. 7:289, 1926.
31. Türk, W.: Beitrage zur kenntnis des symptomenbildes: Polycythämie mit Milztumor und "Zyanose." Wien. klin. Wchnschr. 17:153, 1904.
32. Lange, F.: Ueber Erythrocytose bei cerebralen Lähmungen, Med. klin. 7:1697, 1911.
33. Alexander, W.: Fall von Gehirnthrombose bei Polycythämie, Berl. klin. Wchnschr. 48:1904, 1911.
34. Ledoux, M. E.: Accidents thrombotiques cérébraux dans un cas d'erythrémie. Bull. et mém. Soc. méd. d. hôp. de Paris 48:748, 1924.
35. Alajouanine, Th.; Tzanck, O., and André, R.: Sur les carcteres évoltifs d'un syndrome thalamique au cours d'une érythrémie, Bull. et mém. Soc. méd. d. hôp. de Paris 63:401, 1947.
36. Goldstein, K.: Polycythämie und Hirnerweichung. Med. Klin. 6:1492, 1910.
37. Howell, C. M. H.: Polycythemia. Brain 51:118, 1928.
38. Weber, F. P.: Polycythemia, Erythrocytosis and Erythraemia (Vaquez-Osler Disease). London, H. K. Lewis and Company, 1921, p. 106.
39. Low, J., and Poppen, H.: Beitrag zur Klinik der Polyzythämie, Wein. klin. Wchnschr. 21:357, 1908.
40. Bardachzi, F.: Polyzythämie mit Chorea, Prag. med. Wchnschr. 34:253, 1909.
41. Umney, W. F.: Notes on a fatal case of splenomegalic polycythemia (erythraemia), Lancet 1:1243, 1909.
42. Pollack, L.: A case of chorea and erythremia, J. A. M. A. 78:724, 1924.
43. Doll, H., and Rothschild, K.: Familiäres Auftreten von Polycythemia rubra in Verbindung mit Chorea progressiva hereditaria Huntington, Klin. Wchnschr. 1:2580, 1922.
44. Schiff, P., and Simon, R.: Erythremie avec acces de cataplexie de choré et de confusion mentale, Ann. méd. psychol., 91:616, 1933.
45. Neisser, M.: Fall von Schlafsucht und Hyperglobulie, Berl. klin. Wchnschr. 45: 1206, 1908.
46. Kraus, W.: Pilous cerebral adiposity: A new syndrome, Am. J. M. Sc. 149:737, 1915.
47. Spitz, A.: Das klinische Syndrome: Nerkolepsie mitt Fettsucht und Polyglobulie in seinen Beziehungen zum Morbus Cushing, Deutsche. Arch. klin. Med. 181:286, 1937.
48. Gunther, H.: Uber "zerebrale" polyglobulie, Deutsche Arch. klin. Med. 165:41, 1929.
49. Lhermitte, J., and Peyre, E.: La Narcolepsie-cataplexie, symptôme révélateur et unique de l'erythrémie occulte. Maladie de Vaquez, Rev. neurol. 1:286, 1930.
50. Keschner, M.: Neuropsychiatric complications in diseases of the blood, Internat. Clin. 13:91, 1923.
51. Ferraro, A., and Sherwood, W.: Polycythemia in the course of neuropsychiatric conditions, Psychiat. Quart., 11:19, 1937.
52. Schulhof, K., and Matthies, M. M.: Polyglobulia induced by cerebral lesions, J. A. M. A. 89:2093, 1927.
53. Hecht, P., and Weil, P.: Polyzythämie und Hirnerschutterung. Deutsche med. Wchnschr., 55:380, 1929.
54. Guillain, G.; Lechelle, P., and Garcin, R.: La polyglobulie avec ou sans érythrose, de certains syndromes hypophysotubériens. Ann. méd. 32:100, 1932.
55. Duvoir, M.; Bertraud, I., and Bernard, J.: Lésions encephaliques dans un cas de Maladie de Vaquez, Sang 9:103, 1934.
56. Pitfield, R.: Functional polycythemia and pituitary disease, Med. Rec. 143:416, 1936.
57. Baserga, A.: Poliglobulie da lesioni diencephalo-ipofisarie, Policlinico (sez Med.) 41:17, 1934.
58. Lichtwitz, L.: Hypophysäre Symptome und Hypophysenkrankheiten, Verhandl. d. deutsch. Gesellsch. f. inn. Med. 42:35, 1930.
59. Moehlig, R., and Bates, G.: Influence of the pituitary gland and erythrocyte formation, Arch. Int. Med. 51:207, 1933.
60. Cushing, H.: The Basophil adenomas of the pituitary body and their clinical manifestations (Pituitary basophilism), Bull. Johns Hopkins Hosp. 50:137, 1932.
61. Barker, N., and Craig, W. McK.: Relative polycythemia associated with hypophyseal and diencephalic lesions, Proc. Staff. Meet., Mayo Clin. 11:548, 1936.

62. Salus, F.: Zur zentral-nervosen Regulation des roten Blutbildes, Deutsche Arch. klin. Med. 175:214, 1933.
63. Meiner, E.: Hirngeschwulst und Polyglobulie, Schweiz. med. Wchnschr. 66:338, 1936.
64. Galindez, L. V., and Sanguinetti, L.: Polyglobulia vera with right frontal tumor, Rev. med. latino-am. 19:1055, 1934.
65. Carpenter, G.; Schwartz, and Walker, A.: Neurogenic polycythemia, Ann. Int. Med. 19:470, 1943.
66. Castex, M.: Le rôle du système nerveux centrale dans la régulation de la formule sanguine, Sang 5:641, 1931.
67. Lucia, S. P., and Marasse, H. F.: The central nervous system and hematopoiesis, J. Nerv. & Ment. Dis. 99, 734, 1944.
68. Naville, F., and Brutsch, M.: Les complications cérébrales et médullaires de la maladie de Vaquez, Schweiz. Arch. f. Neurol. u. Psychiat. 4:88, 1918.
69. Adams, L.: Polycythemia vera with special reference to the nervous manifestations, Canad. M. A. J 32:128, 1935.
70. Jackson, E.: Ophthalmoscopic appearances in chronic cyanotic polycythemia, Ophthal. 4:1, 1907.
71. Loman, J., and Dameshek, M.: Increased intracranial venous and cerebrospinal fluid pressures in polycythemia, Tr. Am. Neurol. A. 70:84, 1944.
72. Stewart, P.: Account of a case of splenomegalic polycythemia, Med.-Chir. Trans. (London) 88:221, 1905.
73. Douglas, J., and Eisenbrey, A.: Tuberculosis of the spleen, septic infection, polycythemia, splenectomy. Am. J. M. Sc. 147:479, 1914.
74. Ascher, J.: Polyzythämie und Auge, Klin. Monatsbl. f. Augenh. 53:388, 1914.
75. Cohen, M.: Lesions of the fundus in polycythemia, Arch. Ophth. 17:811, 1937.
76. Parker, W., and Slocum, G.: Report of two cases of chronic cyanosis with polycythemia, including opththalmological examination, Ann. Ophth. 20:72, 1911.
77. Behr, C.: Das Wesen der Augenveränderangen bei Polyzythämie, Klin. Monatsbl. f. Augenh. 49:557, 1911.
78. Axelrod, M., and Epstein, S.: The interrelationship of papilledema and polycythemia, New York State J. Med. 49:939, 1949.
79. Cole, N. B.: Comments on a case of polycythemia rubra vera with autopsy, M. Clin. North America 16:1255, 1933.
80. Bottner, A.: Zur Spinaldruckerhohung und zur Einteilung der echten Polyzythämieformen mit Berucksichtigung ihrer Augenhintergrundsveranderungen, Deutsche Arch. f. klin. Med. 132:1, 1920.
81. Meyer, E.: Neuralgie des Plexus brachialis bei Polycythämie, Deutsche med. Wchnschr. 48:341, 1922.
82. Fetterman, J. L., and Spitteler, D. K.: Vascular disorders of peripheral nerves, J. A. M. A. 114:2275, 1940.
83. Gaisbock, F.: Die polyzythämie, Erg. d. Inn. Med. u. Kinderh. 21:210, 1922.
84. Sturgis, C. C.: Hematology, Springfield, Illinois, Charles C. Thomas, 1948.
85. Crosetti, L.: Policitemia vera ed affezioni degenerative del sistema nervosa, Arch. per le sc. med. 53:96, 1929.
86. Chalgren, W. S., and Johnson, D. R.: Peripheral neuritis due to polycythemia vera, Minnesota Med. in press.

● By the brain I mean all the mass contained within the cranium and which it entirely fills. The weight of this mass in adult white males, varies from 3 lbs. 2 oz. to 4 lbs. 6 oz. troy—the weight I uniformly mean, except when avoirdupois is expressly mentioned.

The brain of men greatly distinguished for their intellectual power is usually large. That of Cuvier was one third larger than an ordinary adult brain. It weighed 4 lbs. 11 oz. 4 drachms and 30 grains; that of Dupuytren 4 lbs. 10 oz. According to Desmoulins the brain decreases in weight after the age of seventy. The female brain is lighter than that of the male, usually from four to eight ounces. It varies from 2 lbs. 8 oz. to 3 lbs. 10 oz. "I never found," says Tiedeman, from whom the above statements are derived, "a female brain that weighed four pounds."

—Amariah Brigham in *An Inquiry concerning the Diseases and Functions of the Brain, the Spinal Cord and the Nerves,* published in 1840.

Newer Drugs in the Treatment of Parkinsonism

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PARKINSONISM has been an important and difficult challenge to the neurologist for over thirty years. Prior to 1918 the disease was confined to a relatively small number of arteriosclerotic cases and treatment was of minor concern. However, since the span of life has been lengthened materially in recent decades, we are confronted by vastly greater numbers of such cases in clinic and private practice. In addition, the encephalitis epidemics of 1918 to 1921 provided an acute phase to the problem.[1] Within the past decade, another large group of ill-defined cases have come to attention as a distinct entity. Although patients exhibit features of the other two groups, they resemble neither the postencephalitic nor the arteriosclerotic type. In the absence of a clear understanding of the determining cause and pathology, the name "idiopathic" has been given to this group. Through these sources, there has been a growing accumulation of cases of parkinsonism and much concern regarding methods of prevention and treatment.

PAST TREATMENT MEASURES

In the wake of the encephalitis epidemics of the early twenties, all major efforts were concentrated on discovering a suitable vaccine to prevent the disease and to check its course and symptoms. In the early thirties it became increasingly clear that the effort was fruitless.[2] Thereupon attention turned to improvising other means to combat the symptoms of parkinsonism.

The potato plant extracts, heralded by Bellabulgara and atropine, gave promise of almost miraculous possibilities.[3, 4, 5] However, they fell far short of original expectations and claims, although they continue to serve as good and useful preparations in the treatment of parkinsonism. The six standard plant extracts in current use are stramonium, atropine,

Surveys conducted at Vanderbilt Clinic and the Neurological Institute, New York City, under the department of neurology of the College of Physicians and Surgeons, Columbia University.

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hyoscine, Bellabulgara, Rabellon and Vinobel. Atropine in an 0.5 per cent solution has special value in postencephalitic parkinsonism,[6] particularly among the younger and earlier cases. It may be used in small amounts in idiopathic cases, but should not be given to patients with arteriosclerosis because of the hazard of glaucoma and circulatory disturbances. Hyoscine is a gentle drug in moderate dosage and is used to good advantage in counteracting excitement and tremor, especially among idiopathic and arteriosclerotic patients. Stramonium is employed in the latter groups for control of both rigidity and tremor. The three belladonna preparations, Bellabulgara, Vinobel and Rabellon, have about equal composition and have almost similar effects in idiopathic and postencephalitic cases. They should be administered in smaller doses in arteriosclerotic cases.

The early forties brought surgery into the therapy of parkinsonism, but thus far it has proved disappointing. In the absence of precise knowledge from the pathologist regarding the location and nature of lesions that produce rigidity and tremor, it has not been possible to know exactly where and what to cut. Under the circumstances, some surgeons operate in the subcortex, others on the lenticular nucleus or the pallidofugal tracts, and still others on the spinal cord.[7, 8, 9, 10] This brings us to the recent era of synthetic drugs in the treatment of parkinsonism.

NEWER SYNTHETIC DRUGS

Within the past three years certain synthetic drugs have come to the aid of patients suffering with parkinsonism. These will be considered individually.

Artane, developed by Lederle Laboratories, has proved more effective than any of the six standard drugs heretofore employed in the treatment of parkinsonism.[11] Table 1 shows the high ratio of favorable results from Artane, and figure 1 expresses these results in comparison with other forms of medication in graphic form.

Artane is piperidyl-phenyl-cyclohexyl-propanol hydrochloride. It is actually a propyl alcohol. In animal experiments it proved to have 50 per cent of the potency of atropine as an antispasmodic and cerebral stimulant, 12 per cent of its potency as an antisialogogue, and only 1 per cent of its potency as a vagus inhibitor. It had no ill effects upon blood pressure, respiration, blood count, renal or hepatic function, sugar metabolism, growth or reproduction in any of the experimental laboratory animals during six months of pharmacologic studies.[12] It was evident, therefore, that Artane possessed large elements of the favorable effects of atropine without any of its dangerous or disturbing components. Upon

TABLE I
RESULTS OF ARTANE TREATMENT

Type of Parkinsonism	Total No. of Cases	Results of Artane Treatment*				No. of Cases on Previous Other Treatment					
		Improved		Unimproved		Encephalitis vaccine	Hyoscine	Belladonna of all forms	Stramonium	Curare	Surgery of brain and spinal cord
		No.	Per Cent	No.	Per Cent						
Postencephalitic	47	34	72.4	13	27.6	0	26	37	7	3	2
Idiopathic	33	25	75.8	8	24.2	2	14	22	5	1	
Arteriosclerotic	37	30	81.0	7	19.0		29	29	17	1	1
TOTAL	117	89	76.1	28	23.9	11	69	78	24	5	3

*8 cases, or 7 per cent, of the series required continuous supplementary treatment with hyoscine and 14 cases, or 12 per cent, required belladonna in one form or another, in addition to Artane. The other 93 cases were gradually changed from all other medication to Artane alone.

completion of laboratory investigations, the drug was tested in a series of 117 patients with parkinsonism during the course of a year and a half. Since these earlier tests, our study has expanded to more than 400 cases, with results closely similar to those found in the original series.

What commends this drug above all others is its remarkable freedom from toxic effects, as well as the high degree of relief it affords patients against symptoms of rigidity, tremor, oculogyria, akinesia and mental depression. Patients turn to it to escape the unpleasant reactions of other preparations. The drug is available in 2 mg. and 5 mg. scored tablets. It can be administered in half or full tablets three, four, or five times a day, with larger doses in younger patients and smaller doses in older patients. Dosage of 10, 15 or even 20 mg. a day is well tolerated. For the control of oculogyria, dosage should start with 15 mg. a day and increase to 30 or even 40 mg.

In about 20 per cent of the patients it was necessary to add hyoscine when tremor was pronounced or one of the belladonna preparations when rigidity was of severe proportions. Artane was well tolerated in all groups, but was found especially helpful in idiopathic and arteriosclerotic cases. Physiotherapy is a valuable adjunct to Artane treatment, as it is to all other forms of therapy. Complete blood count checks in 50 per cent of the patients failed to reveal any abnormal changes. There is no contraindication to the use of Artane. It is safe to employ in patients with hypertension or with cardiac, hepatic or renal disorders. Because of the great need for new preparations, as emphasized by one of the authors a few years ago,[11] the success which has attended the use of Artane is most gratifying.

Parpanit is a new synthetic antispasmodic drug, developed by J. R. Geigy Company of Basle, Switzerland.* Its chemical formula is diethylaminoethyl phenylcyclopentane carboxylate hydrochloride. It was originally imported in the form of 6½ and 50 mg. dragees, but has recently been placed on the market in the form of 12½ mg. and 50 mg. tablets, under the new name of Panparnit.

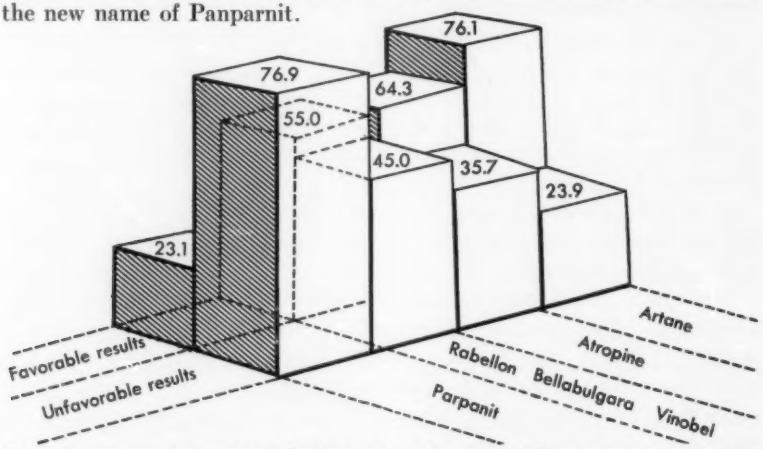


FIG. 1. Percentages of favorable and unfavorable results among different preparations employed in parkinsonism.

The effectiveness of Parpanit was tested in 26 cases of parkinsonism, with results that were far from satisfactory (figure 1). The side-reactions were highly disturbing to arteriosclerotic cases, and those with idiopathic parkinsonism fared only slightly better. While suitably tolerated by post-encephalitic cases, the latter appeared to derive few benefits from it. Parpanit seems to contain some undesirable element in its synthetic structure, as the succeeding reports substantiate.

Domenjoz,[13] in animal studies, found that Parpanit causes a paralysis of the cardiac branch of the vagus nerves, producing tachycardia, suppression of respiration, peripheral vasodilatation and hypotension. With Artane, no such toxic side effects were found in animal experiments. Hartman,[14] who made the original clinical studies with Parpanit in 1946, reviewed his findings in 1947 and reported that its side reactions were so disturbing to the patients that he was forced to discontinue the drug in two-thirds of his arteriosclerotic cases. Bickel and Dubois[15] corroborated Hartman's findings, stating that palpitation, dizziness, uncertainty in walking and other reactions interfere with the clinical use of Parpanit.

*Expressions of gratitude are due the Geigy Co. for providing us with an ample supply of Parpanit for our studies.

Schwab,[16] in 1949, made a favorable summary on the use of Parpanit in 50 cases treated at the Massachusetts General Hospital in Boston. However, examination of his list of toxic reactions from the drug reveals that among his 50 patients, 26 suffered dizziness, six nausea and epigastric burning, four weakness and unsteadiness in the legs, and five feelings of unreality. Furthermore, it is important to note that his series of cases was heavily weighted with postencephalitic patients, who are known to possess tremendous tolerance for any type of drug, even massive doses of atropine.[17, 18]

Advisedly Parpanit should be restricted to postencephalitic cases or may be used in selected idiopathic cases in small dosage, not to exceed 25 mg. t.i.d.

Diparcol is another new synthetic preparation, developed by the Rhone Chemical Society of Paris, in the course of a search for a product with qualities similar to Novocaine. Its chemical formula is diethylamioethyl-N-dibenzoparathiazine hydrochloride. It is distributed in this country by Merck and Company* and is not yet on the market. The product originally came in yellow coated dragees of 50 and 250 mg. size. More recently uncoated scored tablets of 250 mg. were provided which had a burning effect on the throat and had to be put into capsules for some of the patients.

Diparcol was tested on 17 patients. Three of eight postencephalitic patients fared well, but the remainder discontinued its use within a few days or a week because of gastric irritation, nausea, increase in tremor, dizziness or the absence of any effect upon rigidity. Two of four idiopathic cases continued with Diparcol for over six months and claimed greater freedom of movement and bodily comfort. All five arteriosclerotic cases discontinued its use as the result of unfavorable reactions. In our experience, Diparcol proved incapable of substituting for atropine effects in advanced postencephalitics and had little influence upon sialorrhea or oculogyria. It is totally unsuited to arteriosclerotic cases, but has favorable action in mild postencephalitic and early idiopathic cases.

Tolserol is still another new synthetic preparation which has been on the market in England for over two years under the name of Myanesin, but has recently been marketed in this country as Tolserol by E. R. Squibb and Sons. It has the chemical formula orthotoloxy-propanediol. Tolserol comes in 250 mg. tablets and is admittedly ineffective unless taken in large amounts, such as 12, 15 or 20 tablets a day. The patient

*Acknowledgment is due Merck and Company for their generous supply of Diparcol for our studies. We have been recently informed that Merck has discontinued manufacture of this product and has no intention of placing it on the market.

commences with one tablet three times a day and quickly increases to three, four or five tablets three or four times a day.

We followed the effects of Tolserol in 22 patients. While there is an initial curare-like relaxing effect on the muscles in some patients, nausea, precordial discomfort and pronounced increase in tremor led all but one of our cases to discontinue the treatment.

Benadryl, a synthetic antihistaminic derived from ethanolamine, has come to be employed as an adjunct to the treatment of parkinsonism during the past two years. We have used the product among 60 of our cases along with Artane. Close to 30 per cent of patients who had tired of hyoscine found relief in Benadryl against tremor, agitation and insomnia. Patients who complain of unpleasant sleepy reactions should be given the drug only upon retiring. The use of Benadryl should be limited to arteriosclerotic and idiopathic cases, since it seems to have no value in postencephalitic cases. The preparation is marketed in 25 mg. and 50 mg. capsules.

Thephorin is another new synthetic antihistaminic, which was tested for its effects among 10 of our cases. Only one patient seemed to derive benefit in lessening of tremor and rigidity. After six months, the effect wore off and he returned to the previous medication. The preparation has no advantages over Benadryl and is in fact much inferior in effects on patients with parkinsonism.

Curare has been followed by us in 12 cases. This drug is of value only for the release of advanced contractures in postencephalitic cases, preliminary to the institution of vigorous physiotherapy measures. It leads to severely disturbing reactions and ought not be used in arteriosclerotic patients.

CONCLUSIONS

Synthetic drugs have at long last come to the aid of patients with parkinsonism. The new synthetic, Artane, has proved to be more effective and less disturbing to such patients than any of the six standard plant extracts, and far less disturbing than other synthetic drugs. It is so gentle in action that it is safe for both the old and the young, the invalid and the ambulatory, and even among those suffering from hypertensive, renal and cardiac disorders. It is of special value in arteriosclerotic and idiopathic cases, although it has proved useful in postencephalitic cases as well. The antihistaminic, Benadryl, is helpful in the control of tremor and is well tolerated by many patients in small doses. It has proved to be a good adjunct to Artane or the belladonna products in cases where hyoscine is poorly tolerated, or in cases where hyoscine has lost its effect through

long use. Diparcol is of value in a limited range of cases, but its production is being discontinued by the manufacturer. Parpanit is too toxic, but can be used as substitution therapy in selected postencephalitic cases. Thephorin is another antihistaminic that has shown fewer advantages than Benadryl. Although Artane stands out supremely among present remedies, it is hardly the end of the search. On the basis of its successful achievements, hope rises for sufferers with parkinsonism, that in the not too far off future there will be still better synthetics which may ultimately bring complete relief from tremor, rigidity and oculogyria.

REFERENCES

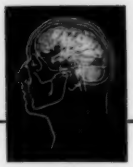
1. Epidemic Encephalitis. Report of a Survey by the Matheson Commission, New York, Columbia University Press, 1939.
2. von Witzleben, H. D.: Methods of Treatment in Postencephalitic Parkinsonism, New York, Grune & Stratton, Inc., 1942, p. 52.
3. Alcock, N. S., and Carmichael, E. A.: An investigation into the treatment of parkinsonism with bulgarian belladonna, Quart. J. Med. 7:565, 1938.
4. Hill, D.: Bulgarian treatment of postencephalitic parkinsonism; A comparison with English belladonna, Lancet 2:1048, 1938.
5. Neal, J.: Recent advances in treatment of epidemic encephalitis, N. Y. State J. Med. 34:707, 1934.
6. Doshay, L. J.: Moderate-dosage atropine treatment of the parkinson syndrome, N. Y. State J. Med. 42:1066, 1942.
7. Browder, J., and Meyers, R. A.: Surgical procedure for postencephalitic tremors, Tr. Am. Neurol. A., 66:176, 1940.
8. Bucy, P. C., and Case, T. J.: Tremor; physiologic mechanism and abolition by surgical means, Arch. Neurol. & Psychiat. 41:721, 1939.
9. Putnam, T. J.: Operative treatment of involuntary movements (tremor athetosis), A. Research Nerv. & Ment. Dis., Proc. (1940) 21:666, 1942.
10. Klemme, R. M.: Surgical treatment of dystonia in 100 cases, A. Research Nerv. & Ment. Dis., Proc. (1940) 21:596, 1942.
11. Doshay, L. J.: Recent trends in the treatment of parkinsonism, Med. Rec. 160:339, 1947.
12. Cunningham, R. W., et al.: The pharmacology of piperdene tertiary alcohols, in press.
13. Domenjoz, R.: Pharmacological research on Parpanit. Schweiz. Med. Wchuschr. 76: 1282, 1946.
14. Hartman, K.: The use of Parpanit in neurological cases, Therap. Umschau 3:163, 1947.
15. Bickel, G., and Dubois, J. P.: Parpanit in the treatment of intentional tremor, Rev. med. de la Suisse Rom. 67:708, 1947.
16. Schwab, R. S., and Leigh, D.: Parpanit in the treatment of Parkinson's disease, J. A.M.A. 139:629, 1949.
17. Bremer, F. W.: High atropine tolerance in postencephalitic parkinsonism. Deutches Arch. f. klin. Med. 149:340, 1925.
18. Doshay, L. J.: Graphic Rigidity Index. J. Mt. Sinai Hosp. 5:451, 1948.

Figure 1 originally published in J.A.M.A., 140:1321, 1949.

● Diseases of the nervous system, like those of the heart, lungs, and larynx, require special means of investigation and treatment. In no department of medical science has progress been more decided during the last decade than in that class of affections considered in this treatise, and undoubtedly a great deal of the advancement is due to the instruments and apparatus by which scientific research in this direction has become practicable.

—William A. Hammond in *A Treatise of Diseases of the Nervous System*, published in 1871.

TREATMENT REVIEW



Practical Considerations in the Treatment of Head Injuries

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FORTUNATELY, for both patient and physician, most people sustaining head injuries recover spontaneously. The role of the neurologist in craniocerebral trauma is to decide if and when some type of medical or surgical intervention will aid or hasten recovery. This decision is not an easy one for the reactions of traumatized brain do not follow the physiological laws established in the normal nervous system. The observer must be alert to the false as well as to the real signs of dysfunction and know how to recognize them for what they are. For this reason, clinical experience must often be relied upon more than rule of thumb. The basis for this judgment —symptoms, signs and technical examinations—will be evaluated critically here in order to arrive at practical criteria for handling the head injured patient.

PRELIMINARY OBSERVATIONS

Unfortunately the information which may be gained by the clinical examination of an unconscious patient is limited, but in the case of traumatic encephalopathy crucial decisions must be based upon it. Therefore, as thorough a physical and neurologic assessment as possible should be made. An initial survey of the vital processes and general physical status of the patient will insure that complicating injuries to other parts of the body are not overlooked. Bleeding from the scalp may be controlled temporarily by a pressure dressing after the head has been shaved. Unless the hemorrhage has been excessive or injuries to other parts of the body are severe, shock is not a complicating factor. If present, it is generally combatted easily by a few hundred cubic centimeters of saline; blood or plasma are rarely required.

Maintenance of adequate pulmonary ventilation is of paramount importance. Frequently, cerebral injury tends to induce pulmonary edema. Aspirated mucus or the patient's limp tongue may superimpose a mechanical obstruction of the airway in the throat. By placing the patient prone with his head turned to one side, secretions will drip out and the tongue

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Presented at a forum on "Trauma" before the American College of Surgeons, Boston, Massachusetts, October 27, 1950.

will fall away from the pharynx. If simple posturing and the use of a sucker is not adequate, an intratracheal tube should be passed immediately. A tracheotomy and tube may be necessary later to keep the airways patent. Adequate pulmonary ventilation is of great importance since even minor degrees of cyanosis and hypoxia cause cerebral swelling[1] which, in an already injured brain, may result in serious and irreparable damage.

Having made certain that the vital processes are in order, attention may be directed to the neurologic status. A detailed account of the accident given by witnesses often gives a clue to predisposing causes for the injury and some idea of the violence of the trauma. If the patient is conscious, his story of the incident will indicate the degree of his amnesia. The amount of both retrograde and antegrade amnesia is related to the severity of brain damage. Status of the central nervous system may be surveyed rapidly by a routine neurologic examination. In a responsive patient the more important points are the state of consciousness, visual fields, optic fundi, size of the pupils and their reaction, extraocular movements, corneal reflexes, sensory status at least in relation to pinprick, ability of the patient to move his extremities, the deep and superficial reflexes and the tone of the neck musculature. If the patient is unconscious, size of the pupils and their reactions, the corneal reflexes, the amount of flaccidity in the limbs and the reflexes may be checked easily. Having made a physical and neurological assessment, the neurologist is in a position to evaluate his findings in terms of severity of the injury, evidence of progressive complicating factors and prognosis.

EVALUATION OF PHENOMENA IN TRAUMATIC ENCEPHALOPATHY

State of consciousness. The primary result of a head injury is an impairment of consciousness, which may vary from a momentary dazed or dizzy feeling to profound coma. How is the degree of impaired consciousness correlated with severity of cerebral injury or the likelihood of complications requiring surgical intervention? Most writers imply that the state of consciousness is a good index to the amount of neurological damage. In assessing the value of consciousness as an indication of severity of cerebral trauma, it is pertinent to discuss the anatomical and physiological basis of the phenomenon. Until recently investigators have considered traumatic unconsciousness due to a paralyzing effect upon all neurones.[2] This view has been challenged by both experimental and clinical studies. Windle and associates[3, 4] found that certain brain stem neurones were more susceptible to trauma than other cells of the central nervous system. Jefferson has held the view that functional integrity of a small area in the hypothalamic region is essential to consciousness.[5] The thalamic reticular system plays an important role in this function, according to Jasper.[6] Jefferson argued that damage to this "waking" center resulted in traumatic stupor which he considered pathological sleep or parasomnia. If this thesis is accepted, and the evidence at this time favors it, one is forced to the conclusion that the degree of impairment of consciousness is correlated with the severity of functional or anatomical damage to this center. Hence the state of consciousness parallels severity of a head injury only if the damage to this

hypothalamic area reflects the general traumatic encephalopathy. In closed head injuries the correlation may be high, since this area is quite vulnerable to stresses exerted on the brain stem as a result of proximity of the rigid tentorium and base of the skull. In open wounds, in which the cerebral stresses seem to be modulated by the fracturing of the skull, the correlation is less. In a group of 246 post-traumatic epileptics, 23.4 per cent stated that they did not lose consciousness at the time of their injury and 12 per cent maintained they were not even confused; these men sustained severe penetrating compound wounds of the head, as is evidenced by the fact that 94 per cent of them had some demonstrable neurological sequelae. It must be concluded, then, that whereas the absence of impairment of consciousness immediately after a blow to the head does not exclude a serious and extensive cerebral wound, a prolonged unconsciousness is indicative of severe injury to the brain stem.

Whereas the initial state of consciousness may not be of great value in assessing the degree of an intracranial injury, post-traumatic changes in consciousness are of great diagnostic import. If the brain is recovering normally from effects of trauma the depth of coma should lessen, but if recovery is impeded by a dural clot the state of consciousness may fluctuate. For this reason changes in the state of consciousness in the period following a head injury are of great diagnostic importance.

The interval syndrome. Since the days of Jean-Louis Petit,[7] a period of consciousness after a head injury followed by a progressive deepening coma has been thought to be indicative of cerebral compression by a dural hemorrhage. The syndrome is produced by many other causes as well. In fact, hemorrhage is responsible for less than 25 per cent of the cases of lucid interval syndrome.[8] Cerebral contusion and edema, fat embolism or pneumatocele may produce this clinical picture, and in some cases no adequate explanation can be found for the syndrome. This may be illustrated by the case of a young child of seven or eight who, while playing, was struck in the corner of the left eye with a rapier. Except for a small laceration he appeared well, but roentgenograms were ordered to see if a foreign body might still be in the orbit. As these examinations were being carried out, the boy lapsed into a coma and within a half hour of his accident was unresponsive and seemed to have a right sided weakness. His history was so typical that a middle meningeal hemorrhage was suspected. As the scalp was infiltrated with Procaine the patient began to stir. By the time the left temporal region had been explored without finding a lesion and the wound closed, the boy was responding. He made an uneventful convalescence. In spite of an air study carried out before he left the hospital, the cause of his transient progressive coma and hemiparesis remained a mystery.

The chances of a dural hemorrhage being present are enhanced if progressive focal signs of neurologic dysfunction are present. The most reliable localizing sign is an ipsilateral pupillary dilatation. As the pupil enlarges, its reaction to light becomes more and more sluggish. Other oculomotor paresis may become apparent as this syndrome progresses. Hemiparesis on the side opposite the dilated pupil is the next most common finding, but paralysis may occur on the ipsilateral side due to compression of the cere-

bral peduncle against the edge of the tentorium. If pupillary and motor signs indicate different localizations, the pupillary are more likely to give the correct position of the clot. As the brain stem becomes further involved decerebrate rigidity appears.[9] If the patient is not seen until this time, there may be no localizing signs since both pupils are usually dilated and fixed at this stage. Unless relief is

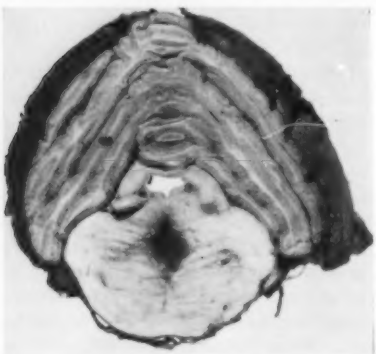

FIG. 1.—A section through the upper pons to illustrate the central hemorrhages usually found in the brain of patients having post-traumatic decerebrate rigidity.

afforded quickly the patient usually succumbs, and at autopsy hemorrhages are found in the upper part of the pons (figure 1).

Although the statistical odds are against a dural hemorrhage as the cause of the interval syndrome, there is no way of eliminating that possibility without trephination. There is no time to lose if the middle meningeal artery is the source of bleeding, for within an hour of injury, decerebrate rigidity, an ominous sign, may herald the approach of death. The following case illustrates this fact. A painter fell from a scaffold to the floor and was knocked out for just a few seconds. He resented the suggestion that he should see a physician but finally was persuaded to have a roentgenogram of his skull made. As this was being done he became drowsy, and within a half hour of injury he was in deep coma. By the time the operating room could be set up, another 15 minutes, he was in a state of decerebrate rigidity and his respirations were of the Cheyne-Stokes type. Fortunately complete recovery followed evacuation of a large extradural clot. The syndrome of the lucid interval is a neurosurgical emergency which may require multiple burr holes if a clot is not found at the initial perforation. Under modern conditions this woodpecker surgery does no harm even if a hematoma is not present.

The compressive syndrome. In the case of a head injured patient who never regains consciousness after the accident, diagnosis of a progressive hemorrhagic lesion is more difficult. It has been taught that the signs of acute progressive intracranial hypertension are falling pulse and respiratory rate and rising blood pressure. Based upon the experimental studies of Kocher[10] and Cushing[11], these have been considered the cardinal phenomena of increasing intracranial tension. But such changes appear only when intracranial pressure approximates the diastolic blood pressure. Moreover these conclusions, derived from animal experimentation, do not seem directly applicable to human traumatic encephalopathy. In man it has been demonstrated repeatedly that changes in pulse rate, blood pressure and respiration do not correlate with apparent intracranial pressure in cases of traumatic unconsciousness.[12, 13] A rather rapid pulse with little alteration in blood pressure is often present in states of traumatic intracranial hypertension. A slow pulse may be

present in the absence of increased tension. It must be concluded that the vital signs are rarely pathognomonic of intracranial bleeding and cannot be relied upon as indications of cerebral compression.

In cases of continuing coma, subdural hematomas are more common than extradural clots, and some authors do not view their presence with alarm, believing that they will be absorbed if the patient survives the primary cerebral insult. It is not possible always to distinguish between extradural and subdural hemorrhages, nor has it been definitely established that acute subdural collections of fluid are benign. Distortion of the brain stem would seem to be, in itself, a factor impeding normal cerebral functioning. Granting that the prognosis in these cases is poor, nevertheless, surgical removal of the subdural hemorrhage seems desirable as early as possible. Here again woodpecker surgery has a place. Moreover if necrotic, lacerated brain is encountered at a polar region, temporal or frontal most commonly, its removal by the sucker will leave an internal decompression and speed convalescence of the patient. If the surgeon encounters an edematous temporal lobe which is compressing the brain stem by herniating through the tentorial notch, he may relieve pressure by cutting the tentorium.

VALUE OF SPECIAL DIAGNOSTIC PROCEDURES

There is no doubt that special procedures may be of value in the diagnosis and prognosis of acute traumatic encephalopathy. Theoretically, they should be applied in every case, but few are practical because of the technical difficulties in obtaining a satisfactory examination. A semistuporous, confused patient who is thrashing about cannot be held still long enough for roentgenograms of the skull, and cannot cooperate in the making of an electroencephalogram. It is more difficult to obtain a satisfactory angiogram. Even a routine lumbar puncture becomes a major procedure in a robust, confused and struggling patient. For these reasons special diagnostic tests in the acute stages of a head injury lose much of their value.

Lumbar puncture. Examination of the spinal fluid in most cases of head injury is of limited diagnostic and prognostic value. Unless the patient is quiet, the pressure of the spinal fluid does not give an indication of the real intracranial tension. Moreover, a normal spinal fluid pressure does not eliminate subdural hematoma; at times, the intracranial pressure may even be subnormal in the presence of a clot. A stiff neck is usually a reliable indication of blood in the spinal fluid, and a spinal puncture only adds confirmatory evidence of the clinical impression. The amount of blood is not always an index of the severity of the injury.[14] Brain stem lacerations or even hemorrhages may be present with little or no blood in the subarachnoid space, and extensive hematomas may occur without appreciable bleeding into the spinal fluid. Repeated spinal punctures cannot be justified on the grounds that they will remove the erythrocytes from the subarachnoid space. Meredith[14] has shown that only a small fraction of blood can be eliminated from the subarachnoid space by lumbar puncture. Yet clinically, considerable relief from a troublesome headache may be obtained by repeated punctures. We must conclude then that, although a lumbar puncture is

advisable in every case of suspected head injury to establish evidence of subarachnoid bleeding for legal purposes, it has little other value.

Roentgenography. It is natural that friends of a patient suffering from a head injury should anxiously inquire if the victim has a fracture. For centuries even physicians considered skull injury to be the most dangerous consequence of a wound of the head, and the ancient surgeon went to great pains to find breaks in the bone. If the fissure were not visible to the naked eye after retracting the pericranium, a sooty oil was rubbed on the skull and the wound inspected the next day for the dark line which would indicate the fracture. This technique, described in the writings of the Hippocratic physicians, was still practiced in the eighteenth century, the only refinement being the use of printer's ink as the impregnating agent.[15] When roentgen rays made it easy to visualize a skull fracture the interest in knowing immediately of a broken bone was revived. However, with rare exceptions, emergency roentgenograms of the skull are not advisable in acute head injuries. Unless the clinical findings suggest a surgical complication of which roentgenograms may give confirmatory evidence, raying of the skull is best deferred until the patient is convalescent when satisfactory films may be obtained easily.

Special roentgenographic techniques such as ventriculography and angiography may be necessary, but in the confused patient they must be made under general anesthesia. Roentgenography of the skull may be said to have limited value in acute head injuries, but in those cases requiring immediate surgical intervention, the findings may be essential to successful operative treatment.

Electroencephalography. Head injury will produce alterations in the electroencephalogram which are dependent to some extent upon the severity of brain damage. Simple concussion causes changes which disappear within an hour, but if an obvious impairment of consciousness is present the electroencephalogram is invariably abnormal according to Denis Williams.[16] Dow, et al.[17] found that, in general, the abnormality could be correlated with severity of injury, but in an individual case this guide was of little diagnostic or prognostic value. As the patient recovers, clinical abnormalities disappear before the electroencephalographic changes which may still be present when the patient is apparently well. Although the brain waves are more often abnormal in patients having skull fractures or blood in the spinal fluid, severe changes may be present without such pathological conditions. If intracranial pressure is increased, the electroencephalographic abnormalities are apt to be more severe.

In the acute stage of head injury, outbursts of abnormal wave forms, such as occur in idiopathic epilepsy, are seen occasionally. Although they may be associated with convulsive attacks, they do not appear to indicate a subsequent post-traumatic epilepsy.[16] Persistence after the convalescent period may be associated with a late-developing epilepsy.[18]

The value of electroencephalography in diagnosis and localization of subdural hematomas is not well established.[19] In some cases, bipolar records from over the effusion are flat relative to monopolar records. Sjaardema and Glaser[20] described high voltage beta waves superimposed on delta waves over subdural hematomas. As asymmetry from homologous areas

may indicate unilateral hematoma. Intracerebral hemorrhage is said to produce localized delta activity.[18]

The use of electroencephalography in acute traumatic encephalography is limited by the usual lack of cooperation of the patient. In the more chronic phases of head injuries, brain waves are both of diagnostic and prognostic importance.

SPECIAL PROBLEMS IN TREATMENT OF HEAD INJURED PATIENTS

Occasionally special problems may arise in the treatment of craniocerebral injuries. Some comment on the general principles of treatment may be of assistance in solving specific cases.

Restlessness. Restlessness often accompanies traumatic encephalopathy and is difficult to control at times. In the period immediately following a head injury, a special nurse may be able to allay restlessness without the use of drugs or mechanical restraints, but the latter should not be withheld if the patient becomes too agitated. During the recovery phase of the head injury, sedatives may be used more freely than in the acute stage. Paraldehyde is perhaps as effective as any drug in allaying restlessness, and the taste and odor are not so obnoxious to the drowsy, confused patient as to a normal individual. Barbiturates such as phenobarbital may be necessary. Morphine should be avoided because of its medullary depressant effect. The following case may illustrate this point. A young woman, sustaining a momentary concussion and a broken nose in a car accident, was treated by a rhinologist. Because of headache and restlessness, she was given a hypodermic of morphine. Some hours later she could not be roused. Except for a bloody spinal fluid, no abnormalities were found on examination. She rapidly deteriorated and died within twelve hours of the injection. At autopsy only a few small cortical petechial hemorrhages were present. Since many similar examples might be cited from the literature, it would seem wise not to use morphine for restlessness following a head injury. Occasionally pain aggravates restlessness. Catheterization of a full bladder or the removal of a small amount of bloody cerebrospinal fluid may relieve an agitated patient. Attention to such complicating factors often brings gratifying results.

Intracranial hypertension. In severe traumatic encephalopathy the spinal fluid pressure is usually increased, although, except in cases of hematoma, tension rarely exceeds 400 mm. of spinal fluid. This intracranial hypertension in head injuries has given rise to considerable concern in the past.[21] For its relief, Cushing,[11] about the beginning of this century, advocated subtemporal depression. For a time this technique was generally used, but in the third decade of the century it rapidly lost favor to more conservative methods. About that time Fay[22] championed dehydration as the treatment of choice in head injuries. Marked restriction of fluids, purging and repeated lumbar punctures constituted the chief elements of therapy, but this therapy did not gain general popularity. When hypertonic solutions were shown by Weed and McKibbin[23] to lower spinal fluid pressure, hypertonic saline[24] and later glucose[25] were employed. However, it soon became apparent that these solutions, producing a secondary increase in pressure, were not very efficient in lowering the intracranial tension.[26] Sucrose, Sorbitol and more recently centrated serum albumen have been

said not to have this defect; however, there is some question of their practical value. Since Quincke suggested lumbar puncture in 1905 as a means of relieving intracranial pressure in traumatic encephalopathy, the technique has been quite popular.[26] Munro, one of the recent strong advocates of the technique, repeats the technique as often as every three hours.[27] But in spite of its popularity, its value has never been conclusively demonstrated.

In recent years emphasis has been laid upon the elimination of dural hemorrhages as a factor in the production of intracranial hypertension, with less concern about brain edema, the assumption being that edematous, contused brain rarely gives rise to lethal intracranial pressures. General conditions conducive to the resolution of edema have been sought. Thus adequate pulmonary oxygenation has been stressed, and the use of antibiotic agents encouraged to reduce the possibility of infection. These conservative methods, with attention to normal fluid and electrolyte balance, have been not only more pleasant for the patient but therapeutically as effective as the more radical techniques.

Rhinorrhea and otorrhea. Bleeding from the nose or ear may only be a manifestation of laceration of the soft part, but usually in cases of traumatic unconsciousness it denotes a fracture of the base of the skull. This implies that a portal of entry to the intracranial cavity is open, whereby bacteria may reach the meninges. In such cases the use of antibiotic agents is advisable for several days after bleeding has stopped. This is true particularly if the discharge becomes serosanguinous and then clear, for the watery matter is cerebrospinal fluid and not, as was thought at one time, a filtrate of serum through a minute fissure fracture.[21] Otorrhea practically never presents a therapeutic problem for it ceases spontaneously usually within a few days. A simple toilet of the external ear is all that is required. The canal should never be plugged with cotton but merely loosely filled so that the fluid may escape freely. In some countries where head colds and sinus infection are common, cerebrospinal rhinorrhea is considered an indication for immediate craniotomy and repair of the dural tear, but in this country, in spite of the frequency of sinus infections, antibiotic and sulfonamide therapy seems to be effective in clearing up the condition within a few days without complications. Only if the rhinorrhea continues for a week, or if signs of menigeal infection are present, need surgical intervention be considered.

Scalp wounds. What influence should the presence of scalp wounds have on the handling of the traumatic encephalopathy? Before the advent of modern antibiotic and chemotherapeutic agents it was considered that wounds of the head should be debrided immediately and closed. With the use of penicillin, however, it is quite safe to postpone surgical procedure for twelve or more hours without increasing risk to the patient. This is particularly advisable if the patient is in shock for any reason or comes in when adequate facilities for a major craniotomy are not available. Once the immediate effects of debridement are safely over, the patient may be treated as one with a closed head injury.

Convalescence. The head injured case responds just as well to early ambulation as any other surgical patient.[28] As soon as he feels able to be

up and around he is encouraged to leave his bed. Occasionally vasomotor responses are impaired and the patient must have the head of the bed raised gradually over a period of days before he can tolerate an upright position. Once up, his activity is increased gradually. Minor headaches or dizziness unaccompanied by neurological changes should occasion no concern. Physical and occupational therapy will aid in rehabilitation. If the patient is engaged in an intellectual occupation requiring quick decisions under stress, it is imperative that he be capable of coping with the situation before he returns to work. Psychological examination may show that his mental capacities are not adequate for the stresses he must encounter. Such circumstances are a frequent cause of depression, anxiety or a post-traumatic syndrome, and a less responsible position may be necessary for a time. Good clinical judgment is the guide in social and economical restoration of the head injured patient.

SUMMARY

The significance of clinical findings in patients suffering from head injuries is discussed critically. On the basis of this analysis, it is apparent that the treatment should be based upon the total clinical picture. Some general therapeutic principles are presented.

REFERENCES

1. White, J. C.; Brooks, J. R.; Goldthwait, J. C., and Adams, R. D.: Changes in blood volume and blood content after experimental concussion, Ann. Surg. 118:619, 1943.
2. Denny-Brown, D.: Cerebral concussion, Physiol. Rev. 25:296, 1925.
3. Groat, R. A.; Windle, W. F., and Magoun, H. W.: Functional and structural changes in the monkey's brain during and after concussion, J. Neurosurg. 2:26, 1945.
4. Windle, W. F.; Groat, R. A., and Fox, C. A.: Experimental structural alterations in the brain during and after concussion, Surg., Gynec. & Obst. 79:561, 1944.
5. Jefferson, G.: The nature of concussion, Brit. M. J. 1:1-5, 1944.
6. Jasper, H.: Diffuse projection systems: The integrative action of the thalamic reticular system, EEG & Clin. Neurophysiol. 1:405, 1947.
7. Petit, J.-L.: Traité des Maladies chirurgicales, 1790, 123 pp.
8. Knighton, R. S.: The interval syndrome. Bull. Los Angeles Neurol. Soc. 9:72, 1944.
9. Woodhall, B.; Devine, J. W., Jr., and Hart, D.: Homolateral dilatation of the pupil, homolateral paresis and bilateral muscular rigidity in the diagnosis of extradural hemorrhage, Surg., Gynec. & Obst. 72:391, 1941.
10. Kocher, T.: Hirnschütterung, Nothnagel's spec. Path. u. Therap. 9 (pt. 3): viii + 457 pp.
11. Cushing, H.: Subtemporal decompressive operations for the intracranial complications associated with bursting fractures of the skull, Ann. Surg. 47:641, 1908.
12. Browder, J., and Meyers, R.: A revaluation of the treatment of head injuries, Ann. Surg. 110:357, 1939.
13. Woodhall, B.: Acute cerebral injuries: Analysis of temperature, pulse, respiration curves, Arch. Surg. 33:560, 1936.
14. Meredith, J. M.: Can the site and degree of injury and the prognosis in head trauma be accurately determined by spinal fluid erythrocyte counts? South. M. J. 34:1043, 1941.
15. Le Clerc, G.: The Compleat Surgeon, London, F. Walthoe, R. Wilkin, F. and F. Bonwicke and T. Ward, 1727, 392 pp.
16. Williams, D.: The electroencephalogram in acute head injuries. J. Neurol. & Psychiat. 4:107, 1941.
17. Dow, R. S.; Ulett, G., and Raaf, J.: Electroencephalographic studies in head injuries, J. Neurosurg. 2:154, 1945.
18. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalographic studies of injury to the head, Arch. Neurol. & Psychiat. 44:328, 1940.
19. Courville, C. B.; Hjartarson, G. D., and Marsh, C.: The electroencephalographic

findings in subdural hemorrhage and hematoma: Review of the literature and report of thirteen cases, Bull. Los Angeles Neurol. Soc. 14:163, 1949.

20. Sjaardema, H., and Glaser, M. A.: The electroencephalogram diagnosis of subdural hemorrhage, Ann. Surg. 1942, 116: 452, 1942.
21. Robert, A.: Mémoire sur la nature de l'écoulement aqueux très abondant qui accompagne certaines fractures du crâne, Mém. Soc. de Chir. de Paris, 1847, 1:563, 1847.
22. Fay, T.: The treatment of acute and chronic cases of cerebral trauma by methods of dehydration, Ann. Surg. 101:76, 1935.
23. Weed, L. H., and McKibbin, P. S.: Pressure changes in cerebrospinal fluid following intravenous injections of solutions of various concentrations, Am. J. Physiol. 48:512, 1919.
24. Fay, T.: The administration of hypertonic salt solutions for the relief of intracranial pressure, J. A. M. A. 80:1445, 1923.
25. Jackson, H.; Kutsumai, T.; Leader, L. O., and Joseph, L. D.: Effect of hypertonic dextrose solutions on intracranial pressure in acute cranial injuries, J. A. M. A. 100:731, 1933.
26. Quincke, H.: Die diagnostische und therapeutische Bedeutung der Lumbalpunktion. Klinischer Vortrag. Deutsche. med. Wchnschr. 31:1825 & 1869, 1905.
27. Munro, D.: The therapeutic value of lumbar puncture in the treatment of cranial and intracranial injuries. Boston M. & S. J. 193:1187, 1925.
28. Symonds, C. P., and Lewis, A.: Discussion on differential diagnosis and treatment of post-contusional states, Proc. Roy. Soc. Med. 35:601, 1944.

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Neurology

Clinical Pathologic Conference

Case Record from the Division of Neurology
Boston City Hospital

Discussion by D. E. Danny-Brown, M.D.

PRESENTATION OF CASE

A 42 year old unmarried stenographer entered the neurologic service on August 7, 1950 because of progressive paralysis of the legs, headache and mental confusion.

The present illness began in January 1950. At that time the patient entered a local hospital because of gaseous indigestion, which was especially troublesome after eating fatty foods, and pain in the right upper quadrant of the abdomen of approximately six months' duration. A cholecystectomy was performed under spinal anesthesia; 1.2 ml. of a solution of Pontocaine (6 mg.) in 10 per cent glucose and ephedrine (0.6 ml. of 5 per cent solution) were injected. Ether and oxygen were administered also. The gall bladder, full of stones, was removed without difficulty. The patient was unconscious for a period of six hours, after which she was found to be oriented and rational. A few hours later she was able to arise from bed, take a few steps and empty her bladder. The following morning she complained of intermittent cramping pains in her calves. During this and the succeeding five days she was unable to initiate voluntarily the acts of micturition or defecation; repeated catheterizations and enemas were resorted to. On the afternoon of the sixth postoperative day there was gradual onset of mild occipital headaches which became increasingly severe; they were accompanied by diplopia. These latter two symptoms lasted only one or two days and disappeared. Recovery of voluntary control of bladder function was said to have been facilitated by administration of Urecholine.

At home, the patient observed that her legs were weak and that the soles of both feet and the buttocks felt numb, "as if they were swollen." She experienced pain in both feet on standing and in the buttocks when sitting. Because of these symptoms her physician advised her to remain in bed, which she did for the next eight weeks without improvement. Pain, which previously had been present only upon weight-bearing, was now present at rest, and had gradually extended from the feet to the legs and thighs. Massage and leg exercises were given during the next four weeks, and pain subsided almost completely. It was easier for the patient to arise from bed and she felt her condition was definitely improved. However, because of persistent muscular weakness, a lumbar puncture was attempted at the patient's home and no cerebrospinal fluid could be obtained. The patient attributed subsequent exacerbation of her symptoms to this procedure. Within a few days, her knees buckled when she walked and her legs became so stiff and weak that she could not get about without support. Cramping pains occurred in the abdomen and were said to be intensified by menstruation.

J. J. Putnam professor of neurology, Harvard Medical School.

When examined in the neurological outpatient department of another hospital in May 1950, it was noted that the patient was well nourished, alert and cooperative and that all cranial nerves functioned normally. There were no motor, reflex or sensory changes in the upper extremities. The legs were very weak and spastic, but she was able to stand erect and the greatest weakness appeared to be in the dorsiflexors of the feet. She swayed very slightly in the Romberg position with eyes closed. Leg muscles were of average size and the tendon reflexes were hyperactive, more so in the left leg where there was sustained ankle clonus. Plantar reflexes were extensor bilaterally and abdominal reflexes were absent. Flexor spasms were observed. Senses of vibration and position were intact, but pain and temperature sensation were absent below T4 on the right side and T9 on the left. The upper border of sensory loss was not sharply defined. There was no tenderness on percussion over the spine; a questionable stiffness of the neck was noted on bending far forward. At this time the patient told of precipitant and at times involuntary micturition.

The patient was admitted to another hospital for further diagnostic procedures on June 15, 1950, by which time weakness of the legs had increased perceptibly, though she could still walk laboriously with short steps. Due to weakness of pelvic and thigh muscles, it was impossible for her to turn over in bed or sit up without the assistance of her hands. Sensory changes were about the same, with touch, vibratory and position senses preserved. The remainer of the examination disclosed no significant abnormalities, aside from the cholecystectomy scar and another one in the right posterior chest wall where part of the ninth rib had been resected previously for drainage of a thoracic empyema. Temperature, pulse, respiration and blood pressure were within normal limits.

Lumbar puncture was attempted on three occasions, but no cerebrospinal fluid was obtained. X-rays of the entire spine and skull disclosed no abnormalities. Blood cell counts and urine examination were negative. A cisternal tap was performed and 3 ml. of Pantopaque was instilled. This material was observed to pass to the level of the interspace between the second and third thoracic vertebrae. The lower border of the Pantopaque column was irregular and serrated; a few drops of opaque material were scattered below this level. Cisternal fluid contained no cells, and the total protein was 16 mg. per 100 ml. The blood Wassermann test was negative.

On June 23 an exploratory laminectomy was carried out at T2 to T4. There were adhesions between the arachnoid and dura at this level and as far above and below as one could see. The wound was closed, and there were no complications except for slight fever on the first two postoperative days. Fragments of dura and arachnoid were submitted for microscopic examination which showed a few neutrophilic leucocytes and lymphocytes, but no tumor cells. By July 14 she was able to walk for short distances with the assistance of a nurse, and she complained of pain less often.

Four days after returning home the patient began to have continuous severe frontal and occipital headaches. Soon thereafter the first of numerous spasms occurred during which all four extremities were extended and the neck and upper spine became opisthotonic. Spasms lasted for a few seconds, and the patient vomited from time to time. Mental confusion became so pronounced that it was impossible for the family to attend to her needs.

Past history: This was noncontributory, except for pleurisy and empyema of the right chest which was drained by thoracotomy eight years previously. Subsequent x-rays of the chest were negative.

Family history: The patient's father had died of carcinoma of the lip at the age of 56.

Examination: When first seen at the Boston City Hospital on August 7, temperature was 98.4, pulse 96, respirations 19 and blood pressure 118/80. The patient

lay with legs flexed at knee and hip and occasionally exhibited brief involuntary flexion movements of one or other leg. The arms were held usually in a position of adduction with flexion of the elbows. She was drowsy, irritable and complained frequently of aching all over. It was impossible to engage her in conversation and she seemed to be unaware of much that was going on around her. Responses were often monosyllabic and not always appropriate. The pupils were 5 to 6 mm. in diameter and reacted normally to light and on convergence. She was able to recognize common objects and noticed a moving stimulus in all quadrants of visual fields. Optic discs were sharply defined and suggestively pale. Arteries were unusually thin. The eyes moved conjugatedly through a full range. Hearing was acute, and no other cranial nerve abnormalities were noted. Voluntary movements of the arms were weak, but coordination seemed fairly normal. Arm muscles were thin but not atrophic, and the patient withdrew her arms from painful stimuli. The lower extremities did not move voluntarily. Attempts to extend the legs passively resulted in increased flexor spasm, and painful stimulation of the lower abdomen induced vigorous extension of the legs. Ankle and patellar clonus were pronounced; plantar reflexes were extensor. Pain and temperature senses were diminished to absent below T3 on the right and T5 on the left, including the sacral segments. Vibratory and position senses were intact in the feet. The patient was incontinent of urine and feces. The neck was rather rigid and she preferred to keep it extended.

Laboratory studies at the time of entry again revealed urine, blood cell counts and N.P.N. to be within normal limits. A lumbar puncture was not attempted.

Course in hospital: The patient was given 2,000,000 units of penicillin per day. Her neurologic status fluctuated. At times, as on August 12, she was unusually alert and gave intelligent answers to questions. When asked on August 14 if she would mind having a lumbar puncture she replied, "I don't care. You may do anything you wish." At other times she was irrational or unresponsive. She continued to have seizures one to several times a day, in which she cried out, the eyes rolled up, her neck became hyperextended; both arms were pronated and extended and the thighs flexed on the abdomen and the legs upon the thighs. She perspired excessively and the pupils dilated and failed to react to light. The spells lasted from 30 to 60 minutes, during which she was either unresponsive or made feeble inappropriate replies to questions; afterwards she remained drowsy and confused for some hours. Dilantin sodium, 100 mg. four times a day, did not reduce their frequency. The optic disc margins became blurred, but there was no measurable papilledema. On August 16 she had another spell and was drowsy thereafter. About 45 minutes later she became comatose and the respiratory rate fell to 6 per minute. Blood pressure was 140/100; pulse was 96-110 and regular in rhythm. Her color was a dusky bluish-red. The eyes diverged and the pupils did not react to light. The arms were flaccid and areflexic, and the legs were spastic with 4 tendon reflexes and Babinski signs. A few minutes later respirations ceased, but the pulse remained strong and blood pressure rose to 200/150. Caffeine, alpha-lobeline and artificial respiration were unsuccessful in re-establishing respiratory function. By 6:00 p.m. cyanosis and mottled lividity appeared; the blood pressure fell to 50/20 and she expired.

Discussion

The onset of this prolonged and progressive neurologic illness appears to date from the operation under spinal anesthesia, seven months before death. Although cramping pains in the lower limbs and some transitory difficulty in initiating urination might be expected in the first days following spinal anesthesia, the occurrence of severe headache and diplopia from the sixth to eighth postoperative days gave warning of some unusual complication. Rapid recov-

ery from these disorders left numbness and pain of the soles of the feet and buttocks and general weakness of the lower limbs which suggested clearly the presence of persistent damage to the lumbosacral nerve roots. Doubtless these disorders were attributed to a toxic effect of the spinal anesthetic. If the attending physician was puzzled by the extension of pains to the thighs in the next eight weeks, their ultimate subsidence in the following month probably reassured him to some degree. Up to this point the disorder might still be held to follow the course expected of regeneration following chemical damage to the sacral nerve roots.

However, there were already several peculiar features to be noted. The pains, related as they were to extension of the limbs, may well have resulted from traction upon inflamed nerve roots. But such pains are not a feature of the persistent sacral anesthesias seen following spinal anesthetics, and in the present case they were associated with increasing weakness of the lower limbs, involving the extensors of the knees so that the patient was unable to stand. Appearance of pains in the abdomen, followed by further weakness which neurologic examination in May disclosed to be spastic in nature, and impairment of pain and temperature sensation up to the mid-dorsal region clearly indicated the presence of a progressive destructive process involving the spinal cord. Examinations in May and June gave no evidence of focal disease of the spinal cord, and at the highest segmental level of abnormality the fading sensory change, absence of root pains or atrophic changes and freedom from signs of vertebral disease would raise some doubt as to the extent of the pathology. The failure of repeated lumbar puncture might suggest some diffuse process obliterating the lumbar subarachnoid space, but the persistence of active reflexes in all parts of the lower limbs and the escape of tactile vibratory and position sense in all parts do not suggest the presence of any complete destruction of any particular part of the cauda equina or lumbosacral spinal cord. The Pantopaque myelogram evidently directed attention to occlusion of the subarachnoid space between the second and third thoracic vertebrae. The exploration on June 23 disclosed adhesive arachnoiditis extending higher than T2 vertebra.

At this point in the history, progression of symptoms and signs from those indicating irritation of lumbosacral nerve roots, to involve later an ascending series of thoracic roots with diffuse superficial damage to the spinal cord, would be adequately explained by a chronic adhesive arachnoiditis. The complete absence of signs of focal damage is striking. The pathologist's report on the biopsy of arachnoidal adhesions indicated only a mild chronic inflammatory reaction. If some indolent infection of the meninges was present, the normal cisternal fluid and the biopsy failed to substantiate it. Biopsy excluded the possibility that an undisclosed brain tumor was seeding into the spinal subarachnoid space. One is led to believe that a progressive scarring of the leptomeninges had followed an initial inflammatory reaction, though there was no known history of meningitis.

The onset of headache and opisthotomic attacks with vomiting and mental confusion clearly indicated a subacute hydrocephalus, and the final observation of the development of papilledema, without focal signs of

localized cerebral or brain stem disease, indicated further activity of a meningeal sclerosing process in the posterior cranial fossa. The hydrocephalus was not relieved and terminated in death in an acute episode.

It is evident that throughout its course the illness was related to a diffuse pathologic process in the spinal, and later the cerebral, meninges. The complete absence of any focal signs makes it extremely unlikely that any localized tumor, abscess or granuloma existed. I would, therefore, discard any diffuse meningeal involvement secondary to such pathology. Though the fibrosis of the arachnoid implies a preceding inflammatory meningeal reaction, the lack of focal lesion leads me to exclude the chronic forms of granulomatous diseases such as tuberculosis, blastomycosis or coccidioidomycosis. The normal cisternal fluid and negative Wassermann eliminate syphilis. It is more difficult to exclude torulosis, especially in view of the earlier pulmonary disease. I take it that there was no indication of continued chronic pulmonary infection. If there was, I would be unable to exclude torulosis, which occasionally has presented a chronic spinal form before becoming cerebral. The normal cisternal fluid and afebrile course do not completely exclude this possibility, though they make it unlikely.

The remaining possible causes of progressive chronic arachnoiditis are few and are in the nature of inflammatory meningeal reactions which leave a scarred arachnoid as a residual pathologic change. The difficulty in this regard is to explain progression of the pathology over a period of seven months. It is remarkable, however, that chronic adhesive arachnoiditis is by nature a progressive disorder, whether spinal, cisternal or chiasmatic. It is well known as a sequel to meningococcal meningitis, but less than a third of the recorded cases have had a previous history of this disease. In such cases attention has frequently been drawn to the long interval between acute inflammation and subsequent symptoms. Bailey[1] has remarked upon the appearance of late symptoms in spite of the proved efficiency of treatment of the initial infection and the absence of evidence of continued bacterial survival. In the remaining cases of progressive arachnoiditis the presumed cause has been previous extradural inflammation or trauma, or unknown.

In the present case symptoms in the first week following spinal anesthesia suggest the presence of a very mild spinal and cerebral meningeal reaction at that time, without fever and with few signs. Nevertheless, the subsequent course of events showed that the meningeal reaction had been widespread from the beginning and had later progressed to meningeal scarring and adhesions. It is conceivable that some very mild and transitory infection had been introduced by the spinal anesthesia, but only spinal fluid studies at that time could establish this. There is no history of fever at the time. With the available evidence I would have to conclude that the initial inflammatory reaction was indeed induced by the chemical nature of the spinal anesthetic.

Clinical Diagnosis: Chronic progressive (spinal and cisternal) adhesive arachnoiditis, secondary to spinal anesthesia.

Final Anatomical Diagnoses:

1) Chronic cerebrospinal meningitis, with
   a) Meningomyelitis (chronic adhesive arachnoiditis)

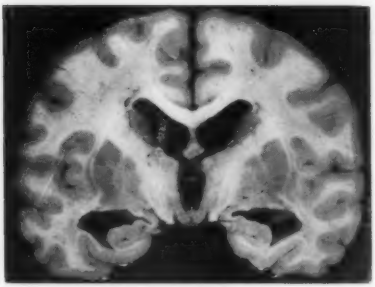

FIG. 1A. Coronal section of brain to show the degree of ventricular dilatation and flattening of the surfaces of the hemispheres.

b) Hydrocephalus

2) Obliterative fibrous pleuritis.

PATHOLOGIC FINDINGS

Gross examination: There were relatively few abnormalities outside the central nervous system. The heart weighed 260 gm. and was not abnormal in any way. Surfaces of the right lung were attached to the thorax by fibrous adhesions. The lower lobe of each lung was congested and subcrepitant, but microscopic sections disclosed only congestion of pulmonary vessels. Liver, spleen, gastrointestinal tract, pancreas, kidneys and endocrine glands were not remarkable. The gall bladder was absent.

Brain was of average size and weight, but the surfaces were flattened and the sulci were narrowed. The arachnoidal membrane was thickened and opaque over the lateral convexities of the cerebral hemispheres, and was grayish-brown over the medulla and pons. The floor of the third ventricle was bulging. There was a slight cerebellar pressure cone. The foramen of Magendie was patent. The foramens of Luschka were obscured by the thickened arachnoid, and water injected into the aqueduct of Sylvius did not flow from them though it did from the foramen of Magendie.

On sectioning the brain the entire ventricular system was dilated to about three times normal size (figure 1A). The lateral recesses of the fourth ventricle were also dilated but not more than the rest of the ventricular system. Walls of the ventricles were smooth and glistening. An adhesion was found between the floor of the fourth ventricle and the posterior medullary velum. No macroscopic lesions were seen in the cerebrum or brain stem.

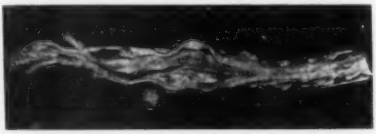

FIG. 1B. The lumbosacral spinal cord and cauda equina. The dura has been incised and separated in places from the thick pia-arachnoid. Roots of the cauda equina are obscured by the thickened arachnoid.

At the site of laminectomy the dura was adherent to extravertebral tissues and greatly thickened (0.4 to 0.5 cm.). Elsewhere the spinal dura was not remarkable except for one small focus of orange-brown discoloration at the sixth thoracic segment. Over the full length of the spinal cord the dura was attached so firmly to the pia-arachnoid that sharp dissection was required to separate these membranes. The pia-arachnoid was exceedingly thick and of grayish color. At the level of the fifth and sixth thoracic segments it was stained a yellowish-brown color. The roots of the cauda equina were of natural color and size but could not be extricated from the sclerotic meninges (figure 1B). On transverse sectioning of the

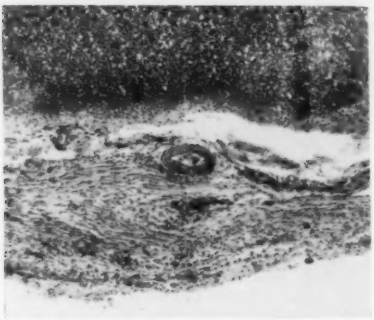

FIG. 2. Hematoxylin and eosin stain of T6 segment of spinal cord to show thickening and fibrosis of the pia-arachnoid.

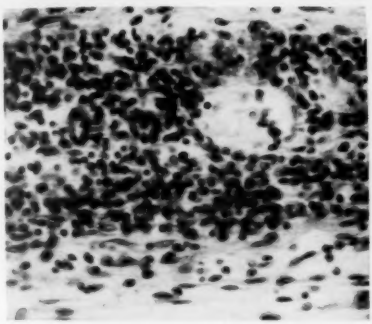

FIG. 1B. The lumbosacral spinal cord and geal infiltration. Owing to thickness of the section, many cells are not in sharp focus but the predominance of lymphocytes and mononuclear cells is evident.

spinal cord one small cavity 0.5 mm. in diameter was seen in the posterior columns of the fifth thoracic segment.

Microscopic examination: Probably the most striking change in the microscopic sections was in the pia-arachnoid. These membranes were thickened by fibrous connective tissue (figure 2). The latter was in the form of heavy bands of collagen in some places and of delicate cellular reticular fibrils in others. Fibroblasts were increased in number and size. In some places the arachnoid and dura were fused into a thick mass of connective tissue; elsewhere they were separated. Cellular infiltrates of lymphocytes, mononuclear leucocytes, plasma cells and neutrophilic leucocytes were scattered through the pia-arachnoid (figure 3). Macrophages containing blood pigment were seen here and there and in large numbers around the aforementioned meningeal hemorrhage. There were several foreign body giant cells in the vicinity of the operative site and an occasional one over other thoracic segments. No parasites, fungi or other organisms could be found in either hematoxylin and eosin or in Gram-Weigert stains. This type of meningeal reaction was most pronounced over the upper thoracic segments, and was of moderate intensity over lower thoracic, lumbar and sacral segments, and of slight degree over the upper cervical segments, medulla and pons. The arachnoid was thick and fibrotic over the foramens of Luschka as can be seen in figure 4. Some of the meningeal blood vessels had slightly thickened and rather cellular walls but all were patent. An occasional spinal, thoracic or lumbosacral, root was damaged (figure 5). In the affected roots medullated fibers were replaced by macrophages, lymphocytes and hyperplastic fibroblasts.

The spinal dura was involved in many places. Near the operative site it was extremely thick. There was a fibroblastic membrane of several cell thicknesses on the inner dural surface in other places. Scattered collections of lymphocytes, mononuclear cells and neutrophiles infiltrated the dura. A mass of granulation tissue was

found on the outer surface at the operative site.

Pathologic changes within the spinal cord were most pronounced in the upper thoracic segments. As can be seen in figure 6, there was a degeneration of nerve fibers, both the axis cylinders and myelin sheaths in the lateral and posterior columns, just beneath the pia. Here many fibers had disappeared, others were dilated, often to three to four times normal size, and degenerating. There were many fatty macrophages among these degenerating fibers. The more central parts of the white matter and the gray matter were intact except for small cavities in the posterior column and the posterior horn at the fifth and sixth thoracic segments. Many activated histiocytes and microgliacytes were seen in the walls of these cavities. A few plump astrocytes were found amongst the degenerating nerve fibers and around the cavities. The anterior horn cells were for the most part of natural appearance. A few of them were swollen and chromatolytic. Figure 6 shows the relatively slight secondary degeneration of the columns of Goll at all levels and the absence of definite descending degeneration of the corticospinal tracts at L5.

No significant changes were noted in the cerebral or cerebellar cortex and white matter. In a few places the ependymal lining was interrupted and a few small flat elevations were caused by hyperplasia of subependymal astrocytes. The choroid plexuses were not remarkable.

Cultures for bacteria and fungi were negative. No attempt was made to isolate a virus.

COMMENT

The dominant feature of this pathologic process was the extreme

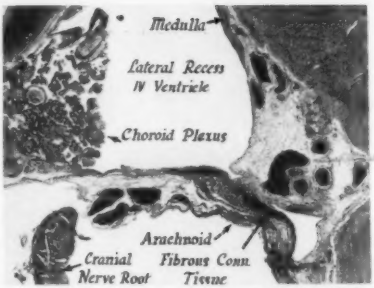

FIG. 4. Hematoxylin and eosin stain of medulla and cerebellum to show the dilated lateral recess of the fourth ventricle and the foramen of Luschka, and slight fibrosis of the arachnoid.

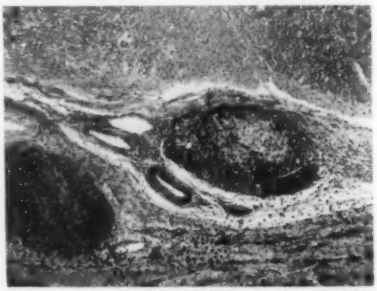

FIG. 5. Hematoxylin and eosin stain of T6 spinal segment. Note degeneration of the central part of the anterior spinal root near center of illustration.

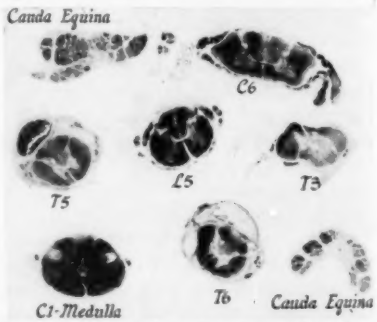

FIG. 6. Loyez myelin stains of several sections of spinal cord and cauda equina. Note the cavity in posterior columns at T3, T5 and T6, the pallor of the posterior columns of T3 and the slight ascending degeneration of the columns of Goll.

fibrosis and the inflammatory reaction in the pia-arachnoid. The subarachnoid spaces over the lower parts of the spinal cord were completely obliterated and this undoubtedly accounted for the failure to obtain spinal fluid by lumbar puncture. The damage to the spinal cord was maximal in the thoracic region and most intense just beneath the sclerotic pia-arachnoid. The lesion within the spinal cord was not of inflammatory type but rather a degeneration secondary to disease of the leptomeninges. In this respect the cord damage resembled that seen in other forms of chronic meningitis, e.g., syphilitic meningomyelitis. The hydrocephalus was either of obstructive or communicating type or both and was clearly related to the obliterative fibrous meningitis. One cannot be certain whether or not the lesion in the thoracic dura, i.e., the granuloma with foreign body giant cells, was part of the original meningeal disease. Presumably it was a reaction to the surgical incision and exploration of this region. The old hemorrhages were probably due to this exploration and to the attempted lumbar punctures.

The symptoms of spinal cord disease are only partly explained by the meningitis over the thoracic cord segments. Considering that spastic paraplegia was quite severe and of three to four months' standing, the relatively slight degeneration of the corticospinal tract was surprising. Here the functional derangement which far exceeded the structural damage may have been related to spinal cord compression. The headaches, decerebrate fits and mental confusion must be ascribed to the basilar meningitis and hydrocephalus. Death was due to the cerebellar pressure cone and medullary compression. Although the hydrocephalus must have been a recent development, the meningeal reaction at the base of the brain seemed to be of the same chronicity as that over the spinal cord.

The postmortem examination provided no clue as to the etiology of the meningeal disease. Judging from the temporal sequence of events, it was initiated by the spinal anesthesia. The delay in onset of neurologic symptoms and the steady progression to a fatal termination within a few months set this type of case apart from the usual spinal anesthesia complication which is believed to be of chemotoxic origin. The type of meningeal inflammation is suggestive of a bacterial or viral infection induced by the spinal anesthesia. Whether or not a chemical irritant can produce a progressive fibrosis of the meninges is not known. This disease process does not differ pathologically from the usual idiopathic chronic adhesive arachnoiditis.

Delayed, progressive damage of the spinal and cerebral meninges following spinal anesthesia is not a great rarity, though it is less frequent than the cauda equina or spinal cord syndrome which occurs immediately after spinal anesthesia. This is the second progressive case which we have examined pathologically in the past year, and at least four or five others have been seen clinically on our wards.

Neuropathologist's report by Raymond D. Adams, M.D., Boston City Hospital.

1. Bailey, P.: Chronic leptomeningeal thickening following treatment of meningitis with sulfa-drugs, Ann. Surg. 122:917, 1945.

Neurology

Official Journal of the American Academy of Neurology

Editor-in-chief: Russell N. DeJong, M.D.
Associate Editor: Webb Haymaker, M.D.
Managing Editor: Margaret M. Kane

Our Purpose

It seems fitting to assume that for the most effective expression of our aims and accomplishments, we, as neurologists, should have autonomy in publications as well as in teaching, administration, and practice. With this in view, the first number of NEUROLOGY is issued under the auspices of the Board of Trustees of the American Academy of Neurology.

There are other media for the publication of articles dealing with neurology, it is true, but their pages are limited and long delays are often necessary. Seventy-six years ago, in the first issue of the CHICAGO JOURNAL OF NERVOUS AND MENTAL DISEASE (later the JOURNAL OF NERVOUS AND MENTAL DISEASE), it was stated, "To discuss the nature, and, according to the best light we now have, the practical management, of disorders of the nervous system, is one of the chief aims of the Editors in projecting their Journal. We do not believe we misstate the real feeling of many members of the profession, when we say they are looking for more information than is easily accessible to them, in regard to the nature and treatment of such diseases."[1] Forty-five years later, in the first number of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, readers were told, "There (is) need of a publication which would keep its readers in touch with the best work of all countries, and which would help to elevate the general standard of knowledge of the nervous system and its disease. Just at this time the need is greater than ever before. The war has been a great school, but many lessons taught need to be—must be—more generally known. The complexities of civil life are increasing, changes are rapid and more are impending. The enormous industrial development in the United States has involved and will involve injuries and diseases of the nervous system. All these things demand research, report, education. In short, the need is for a scientific publication of high ideals which shall not only serve the purpose of the research man and the technical expert, but which shall also be of immediate practical value to the clinician."[2]

These statements apply today just as much as they did at the time they were written. It is not the purpose of our publication to supplant these and other excellent publications, but to augment them and to give us one of our own, restricted to the neurologic point of view. NEUROLOGY is intended to be a medium for the prompt publication of articles dealing with structure, functions, and pathology of the nervous system, including the therapeutic aspects of such pathologic states, and to stimulate individual investigation in these various fields.

R. N. DEJ.

1. Editorial Department, Chicago J. Nerv. & Ment. Dis. 1:71, 1874.

2. Editorial Announcement, Arch. Neurol. & Psychiat. 1:113, 1919.

Cerebral Angiography

P. Almeida Lima, Professor of Neurology, Lisbon Faculty of Medicine. 1950. New York: Oxford University Press, 221 pages, $8.75.

Cerebral angiography was inaugurated by Egas Moniz of Lisbon in 1926 and has now become one of the standard diagnostic methods of cerebral lesions. Lima's book is the first systematic treatise on this subject published by the Portuguese school in the English language. The author has been associated as neurosurgeon with Moniz for more than twenty years, and the combined material of these two investigators comprises more than two thousand angiographies, a number unsurpassed anywhere. Lima corroborates, amplifies and in some cases revises Moniz' fundamental work which had been published previously in the French and German literature. The subject matter is covered in well organized and critical fashion, but unfortunately too little attention is paid to the numerous publications on angiography which appeared in Scandinavian, American and German literature, especially after the war.

After reviewing the history of angiography, its technique is discussed. Lima advocates surgical exposure of the common carotid artery low at the neck in preference to the percutaneous technique now practiced in many centers. He performs carotid angiography bilaterally in one sitting under local anesthesia and obtains routinely three lateral films for each injection (the first film to show the arterial phase, the second the early venous phase, and the third the late venous phase). AP projections are rarely used, and stereoscopic films never taken.

The next chapter deals in detail with the normal arteriogram and phlebogram obtained by vertebral and carotid injection. Then follows a description of the typical displacements and deformities of cerebral vessels caused by intracranial tumors and hydrocephalus. In the next section the angioarchitectonic pattern of cerebral tumors is described. This chapter is particularly interesting and informative since Lima has done much original work on the circulation of meningiomas. The typical double blood supply of meningiomas through branches of the external and internal carotid arteries is discussed, and also the relation of angiographic pictures to modification of the circulation time is analyzed.

The chapter on cerebral aneurysm is relatively brief but vascular malformations are discussed at length.

Angiography offers an important aid in the diagnosis of cerebral vascular occlusion. Special attention is given to the not uncommon thrombosis of the cervical portion of the carotid artery. This condition produces a characteristic clinical syndrome and can be easily recognized by low cervical carotid angiography.

In head injuries, angiography has limited use but it yields important information in the diagnosis of extradural and subdural hematoma. Angiography has little to offer in the differentiation of various mental diseases. The final chapter of the book is devoted to the physiology of cerebral circulation as determined by cerebral angiography.

C. F. L.

The Cerebral Cortex of Man

Wilder Penfield, M.D., and Theodore Rasmussen, M.D., 1950. New York: The Macmillan Company, 248 pages, $6.50.

This book is an elaboration of the Lane Medical Lectures delivered by Dr. Penfield at the Stanford University School of Medicine, San Francisco, in 1947. Although the work of Dr. Penfield on epilepsy and cerebral localization has been followed intensively by neurologists and neurosurgeons for many years, this is the first available summary of experimental and clinical studies carried on at Montreal since 1928 by him and his associates, Drs. Edwin Boldrey, Theodore Erickson, Harry Steelman, and Theodore Rasmussen. It correlates and reviews the records of approximately 400 craniotomies in which the cerebral cortex of the human brain was stimulated while the patient was under local anesthesia.

The subject of localization of function in the cerebral cortex, the most highly developed portion of the central nervous system, has been of prime interest to neuroanatomists, neurophysiologists and clinicians since the middle of the nineteenth century. This book summarizes the most extensive series of studies of such function that has been carried out on the human brain. Individual sections deal with the following aspects of cortical localization: sensorimotor representation of the body, head and eye movement, representation of the autonomic nervous systems, vocalization and arrest of speech, secondary sensory and motor representation, vision, hearing and equilibration, and memory, sensory perception, and dreams.

The conclusions drawn in this book are based upon strictly experimental procedures. The authors have at no time been influenced by preconceived opinions in regard to localization of cortical function. In the discussion of sensorimotor representation, for instance, they show that both somatosensory and somatomotor responses can be elicited by stimulation both anterior and posterior to the rolandic fissure, and then compare the results of such stimulation of both sites. As their work has progressed they have found supplementary and secondary sensory and motor representation. Also, with further investigation, they have found it necessary to designate certain inaccuracies and make changes in the now well known sensory and motor homunculus, first brought forth by Penfield and Boldrey in 1937.

The Cerebral Cortex of Man presents, without doubt, the most thorough and complete study of cortical localization in man that is available at the present time. It is an invaluable contribution to our knowledge of the functions of the human brain.

R. N. DeJ.

NEWSLETTER

Volume 3 • Number 1 • JANUARY, 1951

A. B. Baker, President
Pearce Bailey, President-Elect
Howard D. Fabing, Vice-President
Joe R. Brown, Secretary-Treasurer

AMERICAN ACADEMY OF NEUROLOGY

Academy Meeting April 11-13, 1951 Plans for the second biennial meeting of the American Academy of Neurology are forging to completion. The dates are fixed for Wednesday through Friday, April 11-13, 1951, at the Cavalier Hotel, Virginia Beach, Virginia. . . . Program chairman Dave B. Ruskin has set the stage for an "all-out" meeting. Scientific sessions promise to be both informational and provocative. The social agenda includes a cocktail party Wednesday evening, April 11, and an official banquet Thursday night, April 12. The afternoon preceding the banquet purposely is not scheduled in order to provide one half-day for recreation and sports, relaxation and camaraderie. . . . On another level, the meeting will afford occasion to consolidate the Academy and to pay honor to A. B. Baker, its founder and first president. . . . The 1951 meeting will terminate officially in a joint scientific session with the American League Against Epilepsy Friday afternoon, April 13, but Academy members are invited to remain for the scientific session the following day....Sidney Carter, 710 West 168th Street, New York 32, is the program committee chairman for the League. . . .

Review Course in Neuropathology As previously announced (Newsletter Vol. 2, No. 2), a review course in neuropathology will be conducted at the Cavalier Hotel by A. B. Baker, A. L. Sahs and Fae Y. Tichy for two full days, April 10-11, prior to the 1951 meeting. Material to be covered includes staining techniques, cytology, normal structure and pathologic alterations in neurologic disorders. Evening hours are to be used for reviewing slides with a projectoscope. Special stress will be given to clinical correlations. The fee for the course and loan of slides is $25.00 for junior members, $50.00 for senior members and $100.00 for non-members.

DeJong Represents AAN at Lake Placid At the 61st annual meeting of the Association of American Medical Colleges, Oct. 23-25, 1950, Russell N. DeJong, chairman of our education committee, presented the views of his committee on the place of neurology in the medical curriculum. During this session of medical school deans, DeJong offered recommendations formulated by his committee at a meeting in Chicago (Sept. 17, 1950) with other leaders in neurologic education. Highlighted was a recommendation for autonomous departments of neurology in medical schools.

New Members From Abroad The ramifications of Academy activities abroad are reflected by the addition of distinguished foreign neurologists to its membership. The following honorary corresponding members were elected recently: Prof. Nils Antoni, Stockholm; Prof. A. Austregesilo, Rio de Janeiro; Prof. A. Asenjo, Santiago; Dr. Anthony Feiling, London; Dr. Raymond Garcin, Paris; Prof. K. Henner, Prague; Prof. Knud-Krabbe,

Copenhagen; Prof. T. de Lehoczky, Budapest; Prof. L. de Lisi, Genoa; Prof. Egas Moniz, Lisbon; Prof. G. H. Monrad-Krohn, Oslo; Mme. Le Dr. Sorrel-Dejerine, Paris; Prof. A. H. Schroeder, Montevideo; and Prof. Dr. M. O. Uzman, Istanbul.

Death of F. W. Lewey AAN members were shocked to learn of the death of F. W. Lewey on Oct. 5, 1950, from a coronary thrombosis. Dr. Lewey, who achieved an outstanding reputation in neurology on two continents, was one of the most energetic Academy workers among the senior group. His services as a member of the Board of Trustees and as chairman of the research committee constitute a landmark in Academy history. His contributions to neurology and neuropathology enjoy worldwide acclaim. A complete obituary will appear in the journal.

Legislative Committee Wants Volunteers Russell T. Costello is calling for volunteers to serve on his legislative committee. Previous experience in working with legislators is not essential. Volunteers should write Dr. Costello, 630 Fisher Building, Detroit 2, Michigan.

* * * * * *

New National Institute Holds First Meeting The rising impact of American neurology is delineated by the recent establishment of the National Institute for Neurological Diseases and Blindness. This newly created institute stands as the principal basic research arm of the U.S. Public Health Service for the control of neurologic diseases and blindness. . . . Acting under authority recently granted by Congress and the President, Surgeon-General Leonard A. Scheele has appointed a National Advisory Council for this institute to advise him on the distribution of public funds to non-federal institutions for furthering medical research, training scientific personnel and for the construction of research and training facilities. Members of the council were selected among leaders in education, medicine and public affairs. Also appointed were two ex officio members representing the Veterans Administration and the Department of Defense. Physician members of the council, exclusive of ex officio members, are Doctors George Baehr, Dan M. Gordon, P. F. Lucchesi, H. Houston Merritt, Cornelius H. Traeger, D. W. Woolley and Henry W. Woltman. The first organizational meeting of the council was held at the National Institute of Health, Bethesda, Nov. 16, 1950....Many active projects in neurology formerly listed under other national institutes are to be transferred to the new Institute on Neurological Diseases and Blindness. New applications for research, teaching or training grants will be referred to the Council for review. The next meeting of the council is scheduled for Feb. 16, 1951....

Military Neurology Mounting war tensions place inquiry on the professional status of neurologists joining the Armed Forces. The medical department of the army reports substantial unfilled requirements for neurologists. Physicians with one or more years of training in neurology can be assured of a military classification as neurologists – the Army maintains a separate classification number for neurologists (3128),

distinct from the classification number for psychiatrists (3129). Three-year residency training programs are maintained at Walter Reed, Fitzsimmons and Letterman Army Hospitals.

New Diplomates American Board Sixteen candidates were certified in neurology after examinations held by the American Board of Psychiatry and Neurology in San Francisco, June 1950. The new diplomates are: W. A. Brooksby, Eugene, Ore.; N. E. Carl, Los Angeles; T. W. Farmer, Dallas; W. S. Fields, Houston; D. A. Freedman, New Orleans; H. W. Garol, San Francisco; J. Hoffman, Topeka; L. F. Jenk, Neenah, Wisc.; A. H. Kambly, Ann Arbor; S. L. Pollack, Chicago; C. T. Randt, New York; B. S. Schaeffer, Milwaukee; R. P. Sedgwick, San Francisco; F. D. Stern, New York; W. A. Stephenson, Hines, Ill.; Harold Stevens, Washington; J. W. Wedell, San Francisco; and V. R. Zarling, Minneapolis. . . . A list of successful candidates in the examination held in New York Dec. 18-19, 1950, will appear in the next issue of the Newsletter. . . .

New Department at Georgetown The new department of neurology at Georgetown University Medical Center is developing rapidly under the deft guidance of Francis M. Forster, professor and chairman of the department. The program includes a three-year residency in neurology, with rotation through the Gallinger Municipal Hospital and the Georgetown University Hospital. Training in basic neurology is offered at the Georgetown University School of Medicine and allied institutions. There is an opening for one additional resident.

* * * * * *

Schaller Visits French Clinics Walter F. Schaller recently made a tour of French neurologic clinics and services. Included in the tour were visits to the Salpetriere with Alajouanine and Raymond Garcin and a trip to the Clinic of J. A. Barre at Strasbourg. He also attended a meeting of the Paris Neurological Society. Some of Dr. Schaller's comments: "French neurology is active, highly regarded among the medical profession. The French were just as keen clinicians as ever, attaching primary and deserved attention to this branch of neurology. They are quite alert, however, to the newer procedures of angiography and electroencephalography. In general, I found a good mental and moral tone. . . . I was especially impressed with the fine upkeep of the hospital wards and the general care of patients. The French are very friendly to the citizens of the U.S.A."

O. Foerster Institute A newly created research institute dedicated to the memory of Otfried Foerster has been opened in Detwold, Germany. The purpose of the institute is to further knowledge of the activities of the brain, including an elaboration of the original investigations of Foerster. Doctor F. W. Kroll, one of Foerster's pupils, is the director.

Here and There The VA motion picture "Journey Back," depicting the principles and technics involved in the neurologic rehabilitation of a hemiplegic patient, was awarded first prize at the Eleventh International Exhibit of

Cinematographic Art held in Venice, Italy, Aug. 8-20, 1950. This picture may be obtained on a loan basis from the Veterans Administration. Applications should be addressed to the Chief, Medical Illustration Division, Research and Education Service, Veterans Administration, Washington 25, D.C. Applicants should allow at least two weeks between time of application and expected presentation....A muscular dystrophy research foundation has been chartered by the State of Texas (March 20, 1950) to raise funds for research in this disorder, arouse interest and educate the public. Dr. Albert L. Delaney is president of the new foundation. The address is P. O. Box 384, Liberty, Texas. Among the board of directors are Madelaine R. Brown, Russell N. DeJong, William S. Fields and Henry R. Viets....

Percival Bailey Receives Jacoby Award The first triennial Jacoby Award was received by Percival Bailey, professor of neurology and neurologic surgery at the University of Illinois College of Medicine. This award is made by the American Neurological Association to the member who, in the judgment of a committee appointed by its president, shall have done especially meritorious experimental work upon any neurologic or psychiatric subject during the preceding three years.

The Problem of a Name The California State Medical Society abolished the name "Section on Neuropsychiatry" and established "Section on Psychiatry and Neurology." The VA changed its Neuropsychiatry Division to Psychiatry and Neurology Division. Later the Army followed suit. More recently, during the San Francisco session, the problem of a name was brought before the Section on Nervous and Mental Diseases of the A.M.A. After some controversy, a motion was passed to change the name of the Section on Nervous and Mental Diseases to the Section on Neurology and Psychiatry. At the December clinical session in Cleveland, the A.M.A. Reference Committee on Sections and Section Work disapproved this resolution.

Briefs Walter O. Klingman has been appointed to the Board of Chief Consultants of the Veterans Administration. He is the first neurologist to be appointed to this board....Dr. William S. Sebrell is the new director of the National Institutes of Health, succeeding Dr. Rolla E. Dyer, retired....Dr. David E. Price, formerly the chief of the National Institute of Health division of research grants and fellowships, has been promoted to associate director of the National Institute of Health.... George A. Schumacher has left New York to join the faculty of the University of Vermont College of Medicine as professor of neurology....Cecil L. Wittson has been appointed professor of neurology and psychiatry at the University of Nebraska College of Medicine, Omaha....Royal C. Gray has joined the neurologic staff of the Veterans Minneapolis Hospital....John S. Kapernick of Decatur, Ill., has accepted a post at the VA hospital in Little Rock, Ark....

Percival Bailey

The Neurologic Examination

Russell N. DeJong, M.D., Professor and Chairman of the Department of Neurology, University of Michigan. 1950. New York: Paul B. Hoeber, Inc., 1079 pages, $15.00.

In this volume of over one thousand pages, Dr. DeJong has collected more information related to the clinical neurologic examination than is to be found in any now existent text. The discussion is limited to bedside examination and examination of the spinal fluid, making only cursory mention of technical diagnostic aids. This is far from being a disconnected reference volume. Read from cover to cover, it makes a coherent sequence and is organized to conform with the steps of neurologic diagnosis as performed clinically.

The book is divided into ten parts. Part one concerns the place and importance of neurologic evaluation in the field of medicine generally, and contains a discussion of anamnesis and testing the mental status. One is pleased, at a time when it is "open season" on discovering new "centers of consciousness," to find in this section the statement that disorders of consciousness and memory must be considered an indication of a general rather than a specific defect. Parts two, three and four concern the sensory and motor systems and the cranial nerves, respectively. Each of these sections is prefaced with an up-to-date summary of the pertinent anatomy and physiology. For the most part, this is limited to information directly applicable to the testing which follows. Part five on the reflexes has a broad physiological approach and is very complete. The rather liberal use of proper names to refer to different reflexes and signs is unfortunate, but since many will use the book for reference, it is excusable. The autonomic system is considered at length in part six. Parts seven and eight concern diagnosis and localization in the peripheral and central nervous systems, respectively. Included in these sections are discussions of spinal cord pathology, the low back syndrome, and examination of language functions. Part nine contains a chapter on examination in disordered states of consciousness, and a chapter on malingering and hysteria. The latter is one of the most useful in the book. Part ten is on examination of the spinal fluid.

It is the author's intention to make the work a guide to undergraduate students, as well as to graduate students and specialists in neurology and related fields. It is doubtful if the average medical student could make an adequate selection from the wealth of material presented, however. If carefully chosen for him, certain chapters and descriptions might be appropriate. For the specialist and the postgraduate student in neurology, the book will be invaluable.

A. B. B.

Plasma Clot Suture of Peripheral Nerves and Nerve Roots

I. M. Tarlov, M.D., 1950. Springfield, Illinois: Charles C. Thomas, Publisher, 116 pages, $5.50.

In this small monograph I. M. Tarlov, associate professor of neurosurgery at New York Medical College, has presented the rationale and

technique of plasma clot suture of peripheral nerves and nerve roots.

The technique, which was introduced by Young and Medawar during World War II and perfected by the author, consists first of resecting scar tissue from severed ends of the proximal and distal nerve trunks, then of bringing the two ends of the nerve into apposition and, if the reunion cannot be achieved without tension, making them fast with tantalum wire stay sutures. The nerve junction is covered with liquid antologous plasma which clots to make a neat firm junction. The author presents systematically the data which he has collected on different types of homologous and antologous clots of plasma, fibrinogen, and thrombin and the reasons for his having chosen antologous unmodified plasma for nerve union. He describes special apparatus of his own invention for holding and sectioning the severed stumps of the nerve and for providing a mold for the plasma. The technique for placing tantalum wire tension sutures and for applying the plasma clot is also presented in full detail with clear illustrations. The use of plasma clot in the suture of antologous nerve grafts and in the repair of severed roots of the cauda equina are taken up in later sections.

This book will undoubtedly appeal to the neurosurgeon who seeks instruction as to details of this technique, for the author obviously has had much practical experience with it. It will prove somewhat disappointing to neurologists who would be more interested in the speed and adequacy of regeneration.

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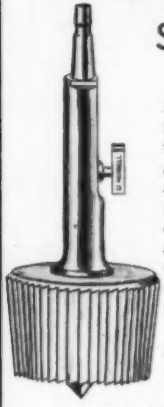

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[1] *U.S. Armed Forces Med. Journal, September, 1950*

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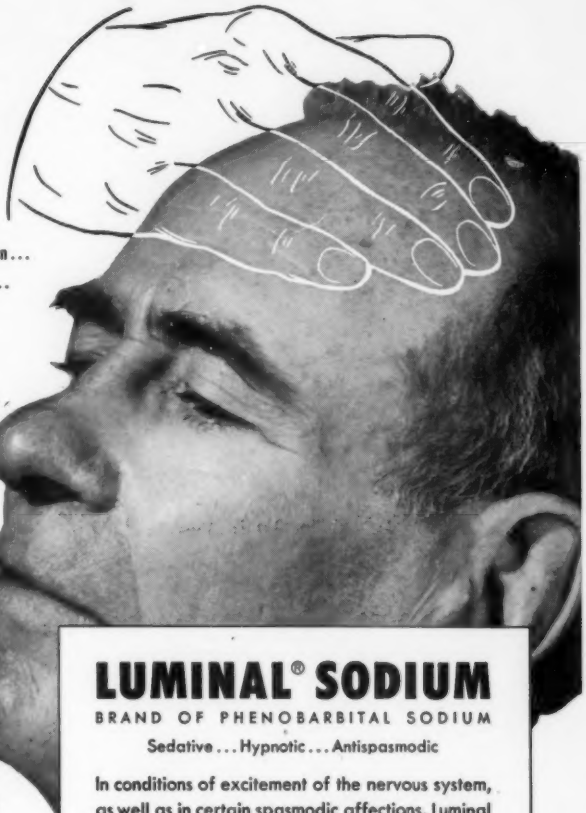

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